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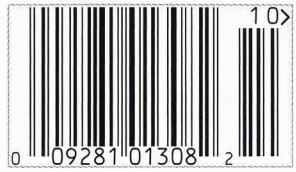

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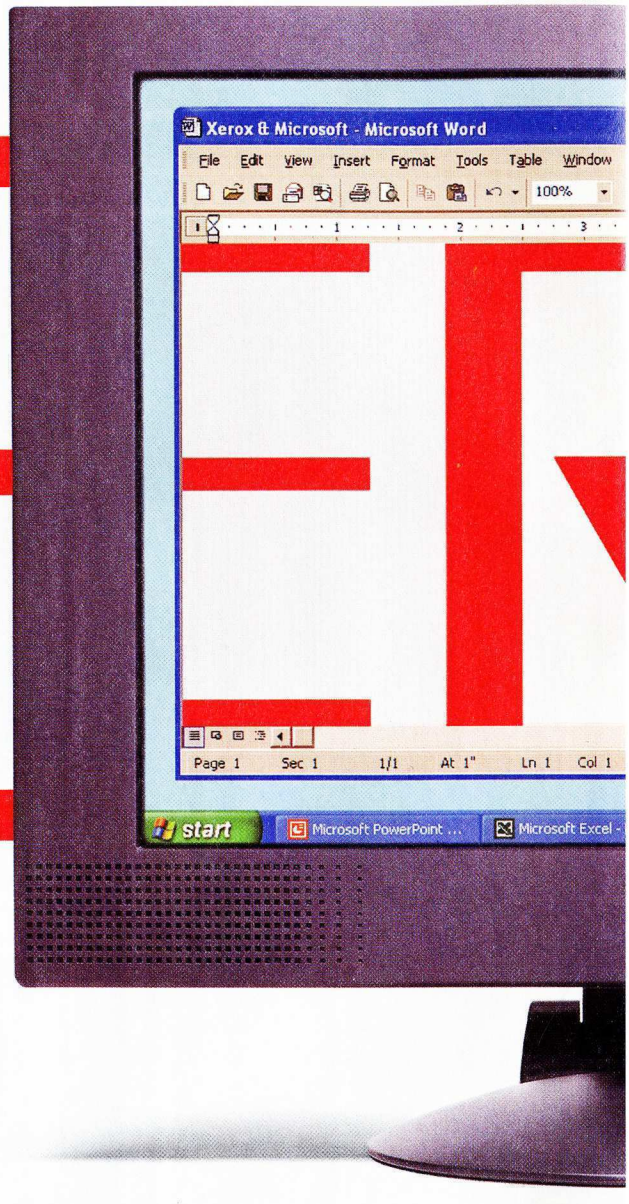

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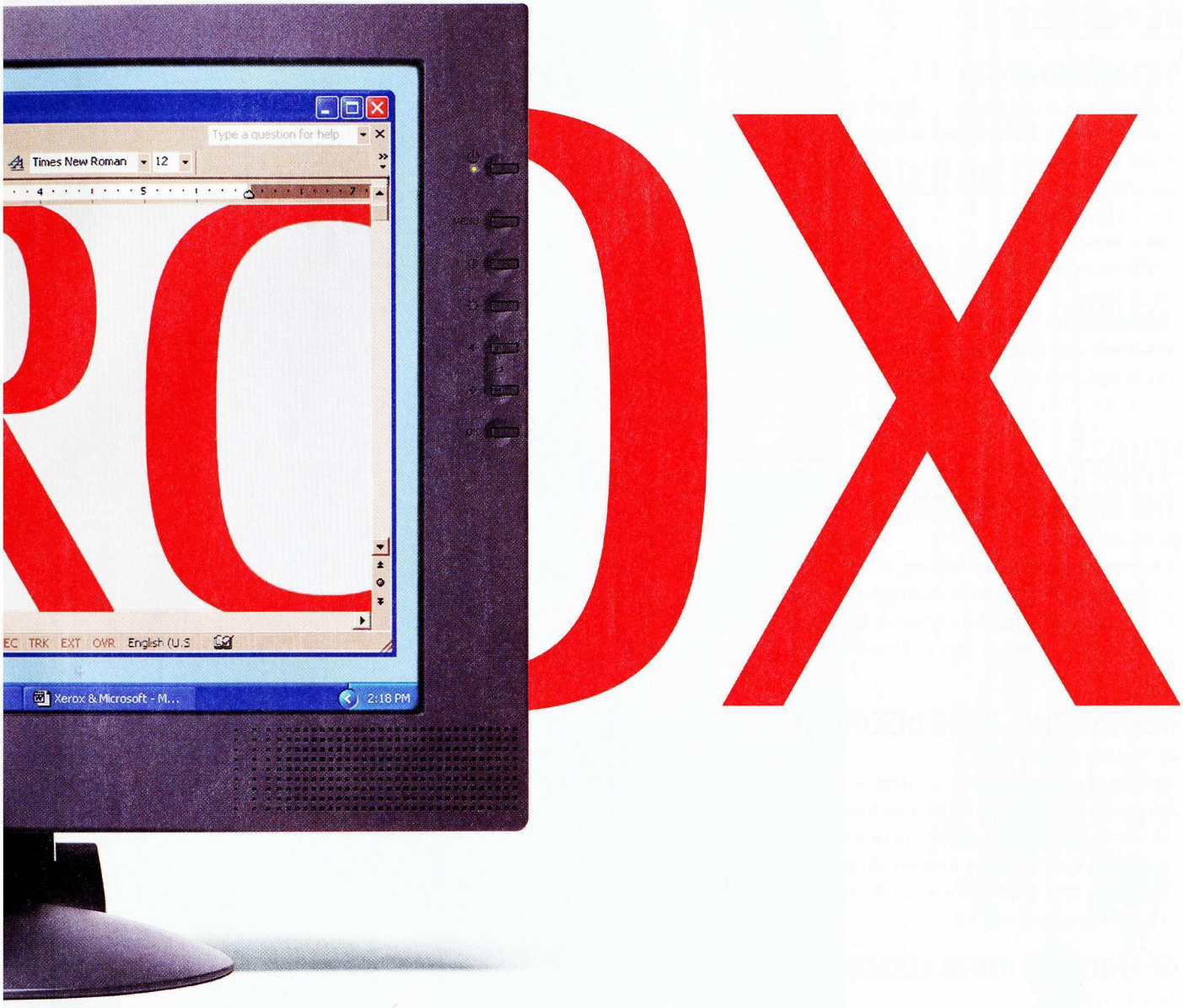

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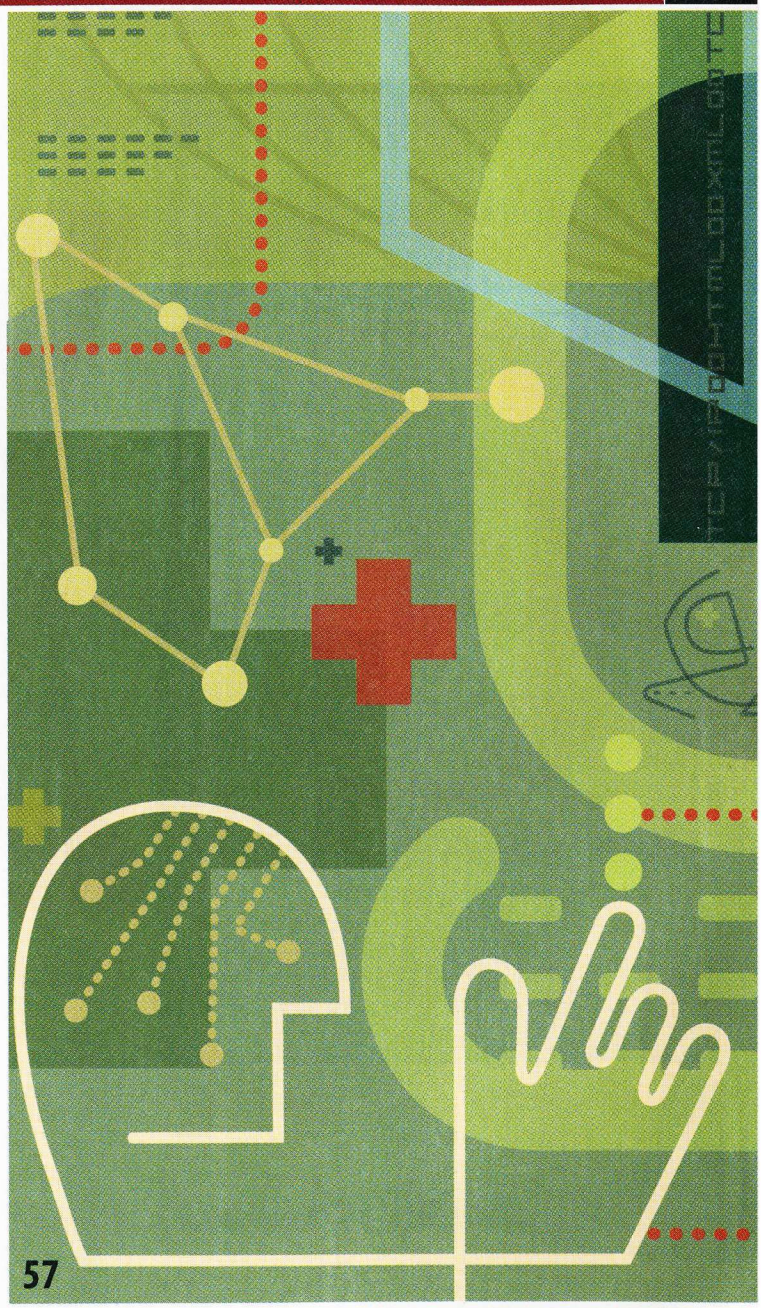

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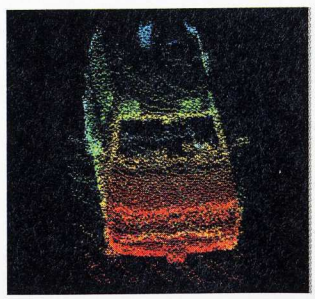
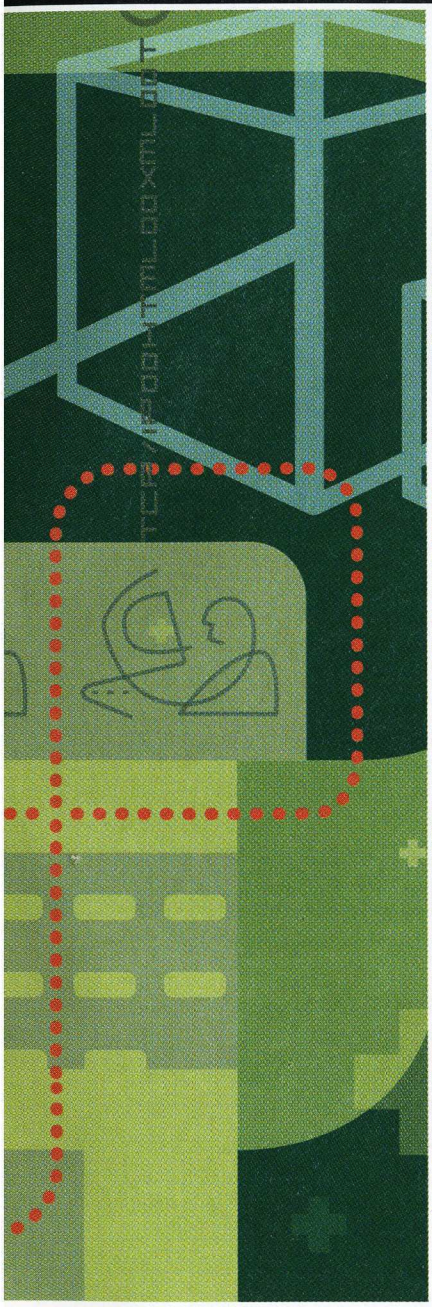
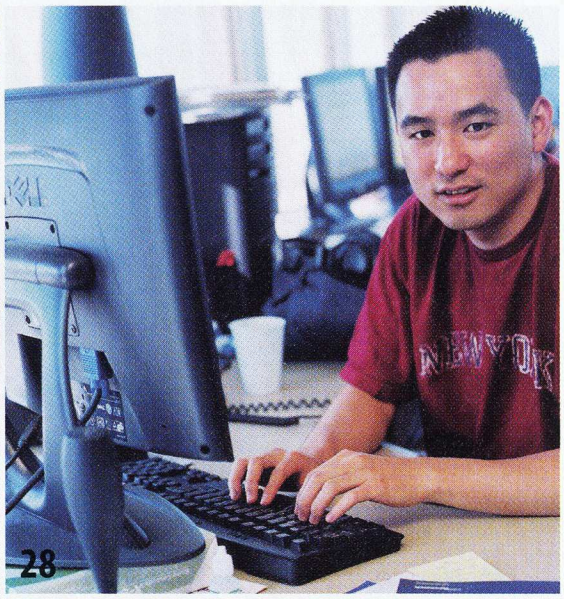


Technology Review
Volume 106, Number 8
October 2003

"The Internet has reached a plateau....The right thing to do is start over."— *p. 28*





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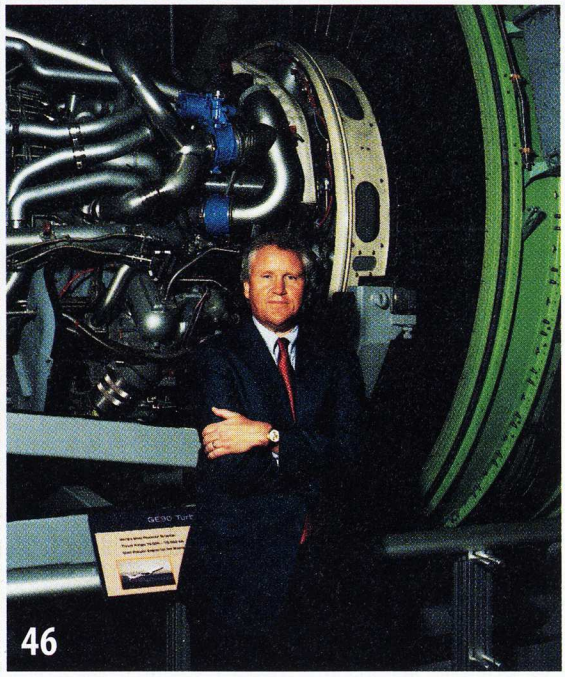
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For breaking stories about emerging technologies and the latest lab advances, visit *TR*'s enhanced Web site. Our three monthly columnists provide analysis and insight into how technology is affecting business and life:
- Richard Muller: Technology for Presidents
- Simson Garfinkel: The Net Effect
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TR Enhanced

WELCOME TO THE LATEST PHASE OF *TECHNOLOGY Review*'s evolution. Nearly six years ago, *TR* embarked on a bold mission: transform a university-run publication with a lackluster circulation of 92,000 subscribers into a vital mainstream technology magazine. We recruited talented editors and writers, photographers and illustrators, and asked them to tell the story of emerging technologies and their impact—on business, society, and personal lives. Today, our circulation stands at 315,000. We have won a slew of editorial and design awards and have been recognized as a National Magazine Award finalist in three of the past five years. In the last year or so, while many biz-tech magazines were going under, we beefed up our Web site, started two newsletters, and worked with leading international publishers to lay plans for four foreign editions, two of which, in Italy and Germany, have already launched. Our global readership is now estimated at more than 1.5 million people a month.

_TR_ has long offered an unrivaled vantage on the future of economic growth. With this issue, we're turning up the heat.

In short, we believe that we have established an unrivaled vantage on the future of economic growth, which is increasingly driven by emerging technologies. And with this issue, we are turning up the heat even more. The reason is simple: times have changed. When *Technology Review* relaunched in 1998, we basked in the light of the dot-com explosion—and anything tech was white hot. Now, it's almost the reverse. But that doesn't change the essential truth: innovation and technological progress are crucial to economic development. Consequently, especially in these less exuberant times, we are determined to work even harder to bring you the important story of technology and its impact.

Our mission hasn't changed. But our focus is sharper than ever, with a renewed emphasis on authority, clarity, and accessibility. You'll find those traits reflected in every section of the magazine, beginning with the cover and its streamlined logo and new tag line. Inside, thanks to a fantastic redesign by outgoing art director Eric Mongeon (who is leaving for marriage and the serenity of western Massachusetts), our typefaces are bolder, the colors more powerful. The features showcase more active photography that does a better job of depicting both the creators and users of technology. You will also find more sidebars, graphs, charts, and tables that serve as different ways to extract the essence of each story. We offer our thanks and best wishes to Eric, while welcoming new art director Linda Koury, who implemented the design with her own flair. Linda was assistant art director at *Fast Company* and art director of *Inc.* We couldn't ask for a better hand-off.

Three new columns will be joining our lineup. One is by Rodney Brooks, director of MIT's Computer Science and Artificial Intelligence Laboratory. As a leading authority on artificial intelligence and robotics, and as head of one of the world's largest and most important computer science labs, Brooks will give *Technology Review* readers a firsthand glimpse into the future of computing. Brooks's column will debut in November. He will then alternate each issue with another new voice: Joe Chung, cofounder of Art Technology Group, one of the original high-flying Internet companies. Chung will turn his shrewd eye toward startups looking for early investors and discuss the broader technological and market challenges confronting these fledgling firms.

The last of our new columns will have a familiar name attached: Simson Garfinkel. An incurable gadgeteer whose column for the past two and a half years has focused on Internet issues, Garfinkel will turn his attention to assessing how technology can fit into, and hopefully improve, people's lives. The column, which he calls "part product review, part how-to guide, part reflection on the impact of technology," debuts this month on page 26 with a look at the rewards and pitfalls of digitizing those paper records in your basement. Only Michael Schrage's monthly examination of business innovation will remain an unchanged part of *Technology Review*'s column lineup.

Even more changes are coming down the pike—and we'll introduce them as we go along. But for now, what better place to start than with our special TR100 issue, featuring 100 of the world's top innovators 35 years old and younger. It's an incredible bunch—with a world of great ideas, and nearly 50 startup companies, between them. (You'll find tables listing the companies in the introductions to our four main sections.) And the TR100 are just part of a lively issue that includes features on an unusual university-industry collaboration called PlanetLab that seeks to engineer a new and vastly improved Internet; the challenges facing pharmaceutical companies striving to refill a sputtering drug pipeline; and a special "Point of Impact" interview with General Electric chairman Jeffrey Immelt, who has beefed up his company's investment in longer-term research in an effort to extend a legacy of invention that traces back to GE's founder Thomas Edison.

Truly innovative organizations never stop evolving to meet changing times. In that spirit, we are very excited about what's afoot at *Technology Review*. We hope you are, too. —*Robert Buderi*

MIT'S MAGAZINE OF INNOVATION

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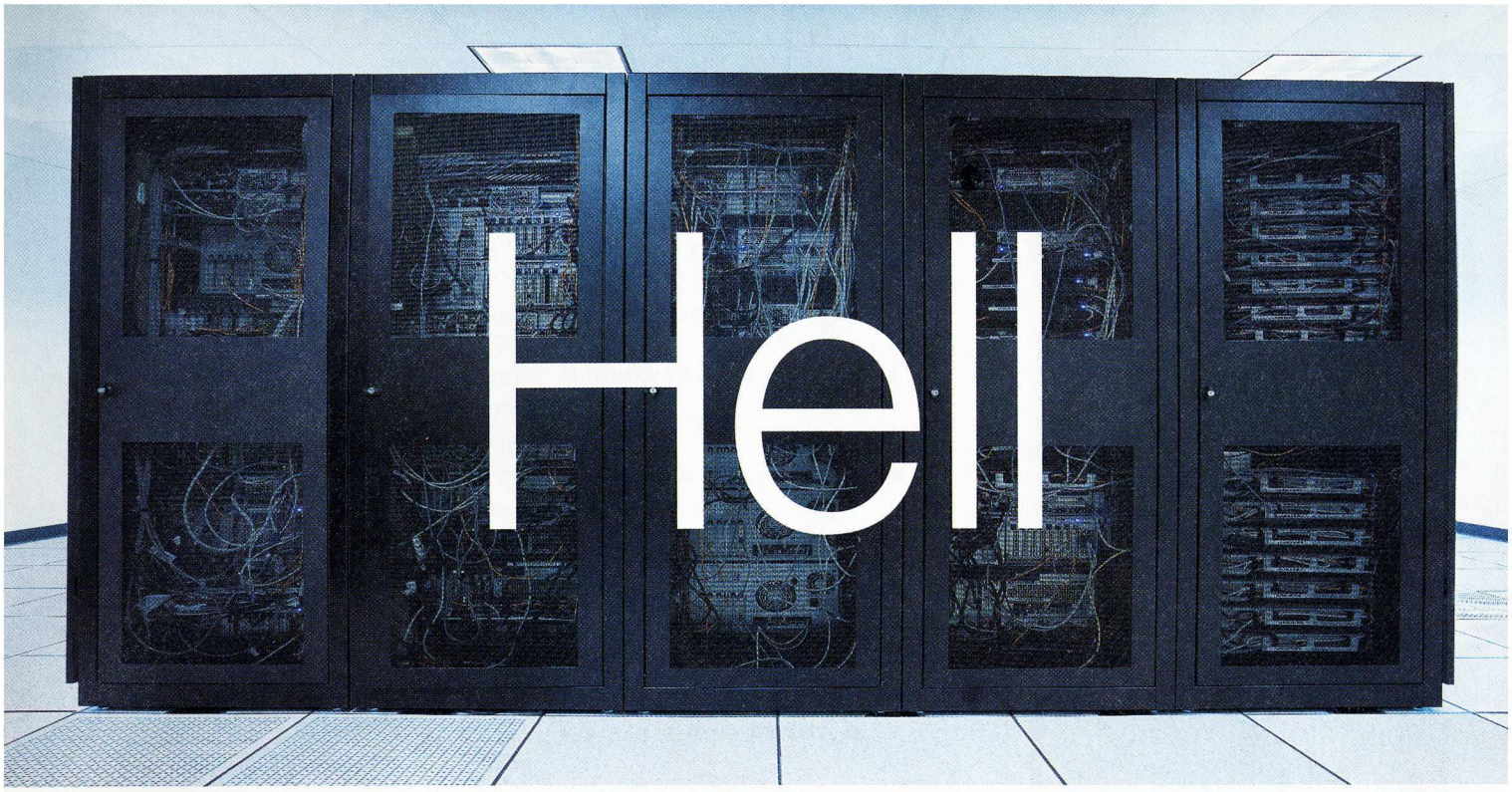

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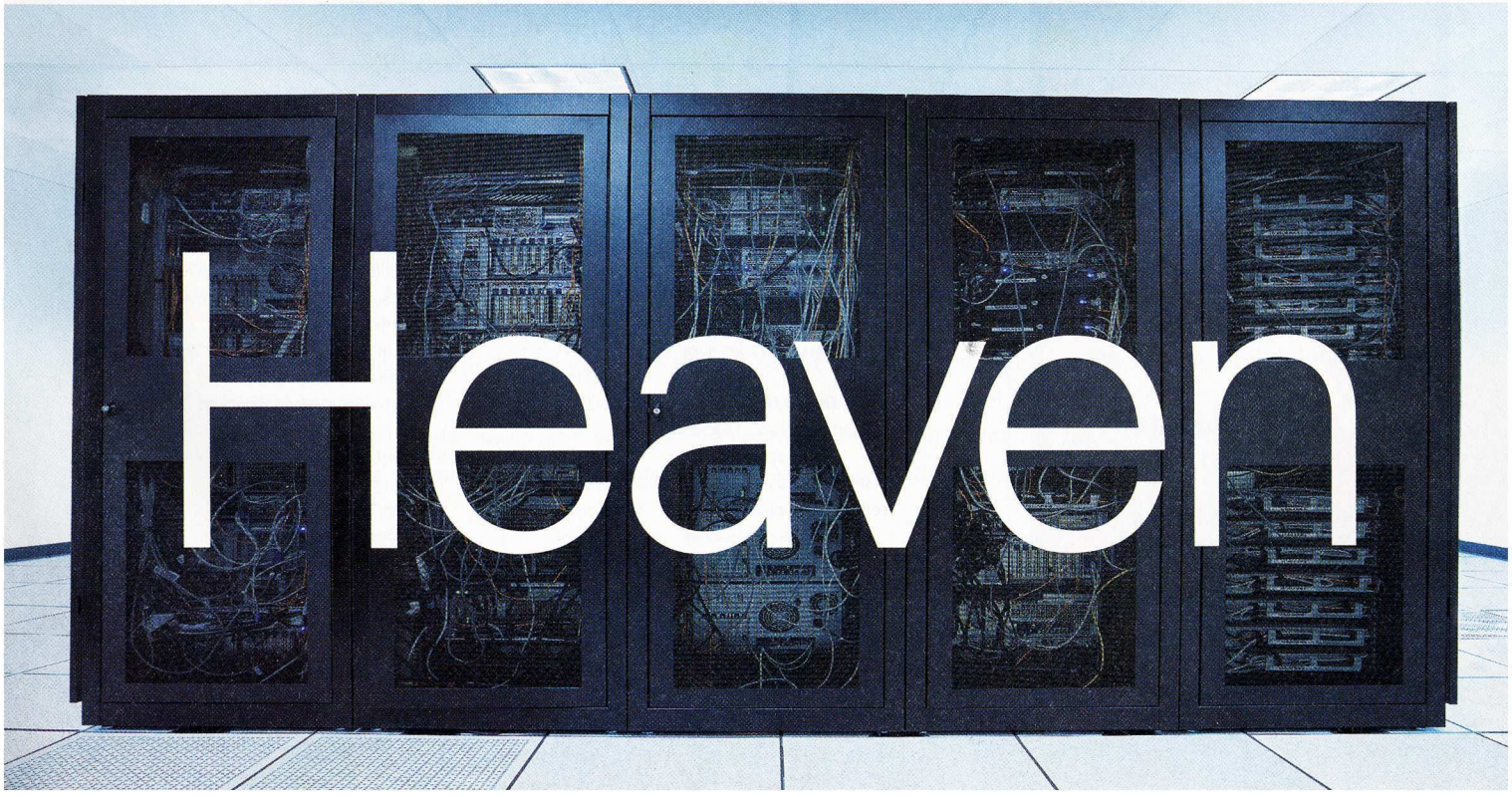

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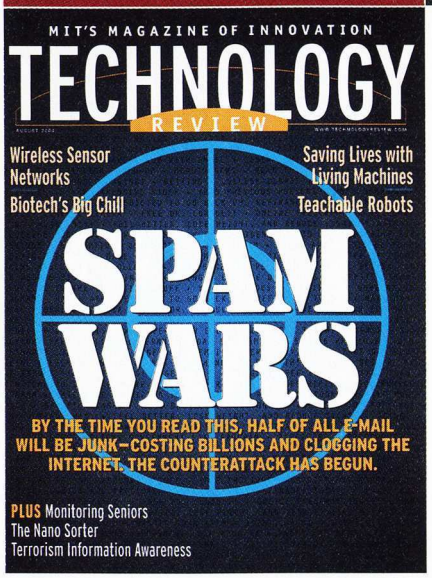

STOPPING THE SPAM

I READ "SPAM WARS" (*TR* JULY/August 2003) and now more firmly than ever am drawn to one conclusion. The only way to cure this cancer is to treat e-mail like snail mail: associate a fee with every message sent. I wouldn't have a problem paying a penny, or even a nickel, for each piece of mail I send. Some unsolicited communications would still get through, but if the sender is willing to spend huge sums of money to send his messages, perhaps those messages are worth reading. Isn't that what advertising is all about?

Richard Iredale
Lake Oswego, OR

IT SHOULDN'T BE DIFFICULT TO WRITE a program to log in to spammers' sites and sign up for services with a bogus ID and credit card, and to repeat this action a few thousand times. If everyone who gets a piece of spam invokes such a program, the provider's server will be effectively blocked from the Internet.

Gene Eplett
San Francisco, CA

FOR EVERY TECHNICAL FIX THERE IS a spammer's workaround. One needs a social fix that makes spamming worthless. Here's an idea: empower a federal agency with special credit card numbers with which to "buy" merchandise from spammers. Then, if banks automatically freeze withdrawals from the receiving accounts, spammers will find a financial disadvantage to using spam as free advertising. If they wanted some fraction of the money, they would have to plead their case and reveal their identities.

Carl David
Storrs, CT

THE ONSLAUGHT OF SPAM SUGGESTS a tailor-made answer to our current budget deficits: impose a tax on any e-mail that is not expressly subscribed to or part of a known list of senders. Wasn't the Internet significantly developed by the government? It's as if we created an

"When taxation of a nuisance can raise badly needed dollars and serve a public good, we've got to get serious about it."

interstate highway system and didn't make the heavy truckers pay fuel and other taxes for pounding our highways into washboard. I'm one of the most antigovernment people you will find, but when taxation of a nuisance can raise badly needed dollars and serve a public good, we've got to get serious about it.

Larry Callahan
Saint Louis, MO

CHILLING RESEARCH

I AM OVERJOYED THAT THERE ARE restrictive measures in place concerning matters of biotech science ("Biotech's Big Chill," *TR* July/August 2003). I am for any policy that restricts a Ted Kaczynski type from gaining access to material that could kill hundreds or even hundreds of thousands of Americans. If the biotech industry must sacrifice profit for America's safety, then so be it: freedom has a price. When we can confidently verify that the people who are gaining knowledge on development of biotechnology are not returning to a hostile nation and using it for aggressive purposes against the United States or a friendly nation, then we can loosen the restrictions.

Eric D. Miller
Tequesta, FL

YOUR ARTICLE "BIOTECH'S BIG CHILL," along with the editorial "Technological McCarthyism," hit a lot of nails on their heads. The people who seek to restrict scientific research in order to thwart terrorists would ban the wheel to prevent car bombs. Brave scientists such as Ariella Rosengard must be allowed to conduct their research and exchange ideas freely. Science's benefits have always surpassed the nightmare scenarios conjured up by critics. The global history of government security programs is a bit more frightening.

Warren Redlich
Albany, NY

LITIGATING LIVING MACHINES

YOUR ARTICLE "SAVING LIVES WITH Living Machines" (*TR* July/August 2003) neglected to discuss the most important factor shaping this field: fear of litigation. Although a federal law protects raw-material suppliers from liability in medical-device litigation, it has never been tested in court, and few big companies want to be the guinea pig. Because of the potential for catastrophic legal costs and liability, most major chemical and materials companies have withdrawn from this market. Yet these are the very institutions with the intellectual resources that can best serve the field.

Donald F. Lyons
Wilmington, DE

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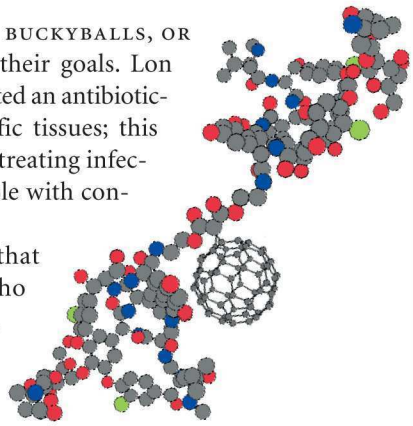
BUCKYBALL ANTIBIOTICS

SOCCER-BALL-SHAPED MOLECULES CALLED BUCKYBALLS, OR fullerenes, could soon help antibiotics find their goals. Lon Wilson, a chemist at Rice University, has fabricated an antibiotic-fullerene complex that's able to target specific tissues; this new type of molecule opens the possibility of treating infections with far greater efficiency than is possible with conventional drugs.

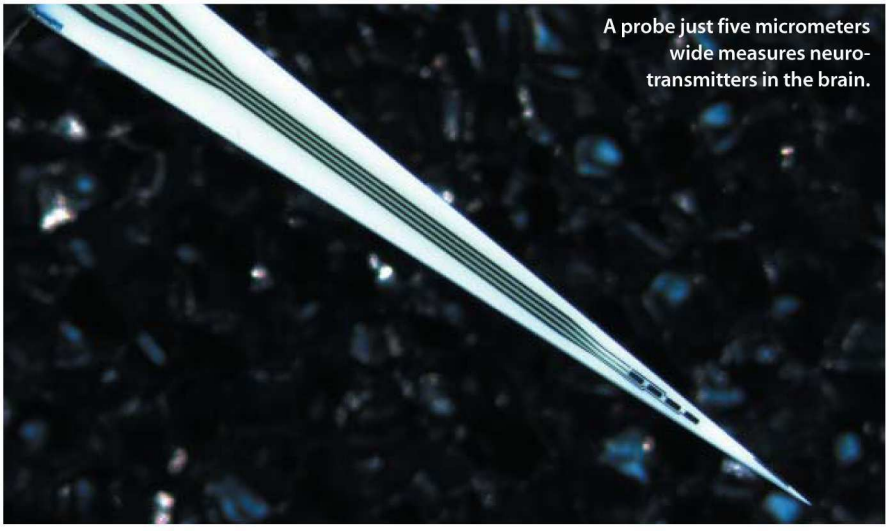


Antibiotic molecules can be attached to a buckyball to target infections.

To treat the bacterial bone infections that occur in a small percentage of patients who undergo orthopedic surgery, for example, Wilson attached two molecules of a potent antibiotic called vancomycin to a fullerene molecule. Then, at a different site on the buckyball, he attached another chemical, which binds only to bone. Because the treatment, which was developed in collaboration with an orthopedic surgeon at Beth Israel Hospital in New York City, precisely targets just the tissue that's affected by the bacteria, patients wouldn't need as large a dose of the antibiotic to treat their infections. Wilson hopes to test the new antibiotic in animals in the next year. He is also working on buckyball versions of the antibiotic Cipro for treating anthrax infections. Such drugs could latch on to anthrax spores in the lungs and destroy the pathogen before it releases its toxin.

CALMER SKIES

In-flight turbulence is hard to predict and the leading cause of injuries on airplanes. Researchers at the National Center for Atmospheric Research in Boulder, CO, have developed software to improve turbulence prediction. When flying through storms, pilots use onboard Doppler radars to scout for drier areas, assuming that these will be calmer. But turbulence can still strike. Algorithms in the new software reduce noise in the radar data; warning algorithms then analyze the data to find the amount of movement in the tiny bits of water and ice found even in "dry" areas. The wider the spectrum of velocities among the droplets, the more likely an encounter with turbulence. In flights on a NASA test plane, the software detected about 80 percent of turbulence with at least a minute's warning—enough time to seat passengers and flight attendants and clear aisles.



A probe just five micrometers wide measures neurotransmitters in the brain.

MIND READER

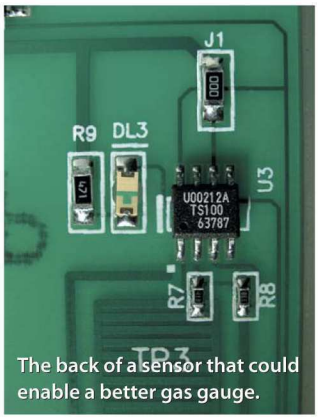
MANY DISORDERS OF LEARNING, MEMORY, AND MOTOR CONTROL ARE CAUSED by abnormal amounts of glutamate, a neurotransmitter in the brain. If glutamate concentrations could be accurately monitored, surgeons could find and remove cells that poorly regulate glutamate levels. So a team led by University of Kentucky neurobiologist Greg Gerhardt has developed microsensors that track the concentration of glutamate quickly enough—and in enough locations simultaneously—to aid in such surgeries. Each sensor consists of at least two recording patches of platinum, coated with an enzyme and polymers, on the end of a ceramic probe five micrometers wide. The coating reacts with the glutamate, creating an electric current proportional to the glutamate concentration. The sensors work on a second-by-second basis, unlike existing devices that take tens of seconds to register changes, says Gerhardt. Placed in an epileptic patient's brain for the duration of surgery, a 60-micrometer-by-700-micrometer array of the sensors could pinpoint the smallest region of tissue that needs to be removed. Gerhardt plans to mass-produce the sensors in about two years at his company, Quenteon, in Lexington, KY.

SHOE SENSING

MOST AIRLINE PASSENGERS AGREE that few things are more annoying than removing their shoes for security x-rays, but researchers might have found a way to speed the footwear check. MIT electrical engineer Markus Zahn and research assistant Jason Sears are developing a shoe-bomb detector embedded in a floor pad. When a passenger steps onto the pad, a series of electrodes generates a low-energy electromagnetic field a few centimeters high that penetrates the soles of the shoes. In less than a second, sensors in the device measure the changes in the field due to the footwear; that "signature" is compared to database-stored signatures for explosives and other dangerous substances. Working with Jentek Sensors in Waltham, MA, the MIT researchers hope to market the technology within two years.

A floor pad could speed airport shoe checks.

COURTESY OF JASON SEARS (SHOE SENSING); COURTESY OF PETER HUETTL (MIND READER); COURTESY OF RICE UNIVERSITY (BUCKYBALL)



The back of a sensor that could enable a better gas gauge.

OUT OF GAS?

YOUR CAR'S FUEL GAUGE IS ON "E." SHOULD YOU STOP FOR GAS, OR CAN YOU EKE OUT A FEW more kilometers? You can't know for sure, because the mechanical floats used in most automobile gas tanks are imprecise. But a cheaper, more durable type of fuel gauge, based on technology used in flat electronic keypads, could tell you exactly, with digital accuracy, how much fuel is in your tank. The pads, based on technology from Wheaton, IL-based TouchSensor Technologies, consist of electrodes mounted behind a plastic plate that create an electric field above the plate. Liquid sloshing over the plate interrupts this field, tripping a switch. Material Sciences, in Elk Grove Village, IL, has licensed the core technology and plans to further develop and market the pads to Detroit automakers, which could embed vertical columns of the devices into the walls of gas, oil, coolant, or windshield wiper fluid tanks; the pads would sense falling fluid levels and transmit precise data to a dashboard display. And because the devices could be placed directly in the walls of plastic tanks as the tanks are molded, they should be cheaper than mechanical-float systems as well.


Electronic tags might help suppliers avoid spoiled food.

TEMPERATURE TAGS

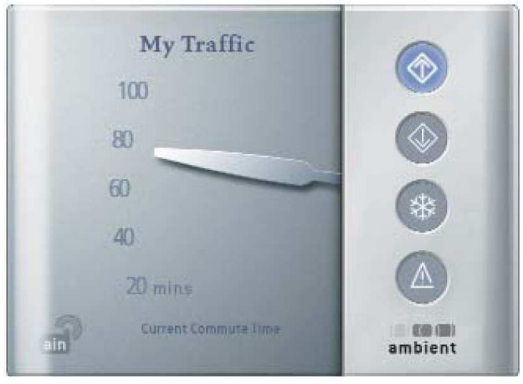
EACH YEAR, BILLIONS OF DOLLARS ARE WASTED IN THE UNITED STATES BECAUSE food, drink, and drugs grow too hot or too cold during transport. Researchers at Infratab in Oxnard, CA, have developed electronic tags that track time and temperature for such perishables as vaccines and meat. Ranging in size from a postage stamp to a credit card, the battery-powered tags are programmed with data on the relationship between temperature and shelf life for specific items. Measuring the temperature every 15 minutes, a tag shows the approach of an item's expiration date by turning a liquid-crystal display from green to yellow to red. This method is more reliable than conventional date stamps, chemical-based labels, and temperature probes mounted in trucks, says Infratab CEO Terry Myers. And retailers can access the temperature history of any tag by scanning it with a computerized radio frequency reader. Companies that ship meat, beer, and pharmaceuticals are testing the tags, which cost from several cents to several dollars each and should be commercially available within a year.

GENE REPAIR

Though facing high hurdles, gene therapy remains the best long-term hope for treating many genetic diseases. But for some devastating disorders, such as polycystic kidney disease, simply supplying patients with healthy copies of their disease-causing genes—the traditional approach in gene therapy—may not be enough. Molecular geneticist Al George at Vanderbilt University in Nashville, TN, has demonstrated a type of gene therapy that can repair the damage caused by such diseases. George created a gene that encodes an RNA enzyme that can excise defective portions of mRNA molecules—short templates that translate a gene's code into a protein—and replace them with the correct sequences. He showed that after injection with the new gene, cells carrying a mutated gene that causes a muscle-wasting disease stopped producing the harmful protein and began producing the normal one. George hopes to improve the process enough to begin animal studies within two years.

CLOCKING TRAFFIC

IT'S QUITTING TIME, AND YOU WANT TO KNOW WHETHER TRAFFIC CONditions will allow you to get home in time for dinner. You could check commuter sites on the Web or listen to the radio—or, as soon as next year, you could glance at the "traffic meter" on your desk. Under development by Ambient Devices in Cambridge, MA, the meter features a dial that might point to "30 minutes" if traffic is light and "90 minutes" if there's a pileup. The meter uses an internal pagerlike device to get updates every few minutes from a computer at Ambient, which both stores a description of your route home and calculates drive time using real-time data from national traffic information systems. The meter is one of a series of "glanceable devices" planned by the company. "We are trying to make all kinds of information as easy to know as time," says Ben Resner, Ambient's cofounder and vice president of technology.



Tracking traffic could be as easy as telling time.

COURTESY OF AMBIENT DEVICES (CLOCKING TRAFFIC); CORBIS (TEMPERATURE TAGS); COURTESY OF MATERIAL SCIENCES CORPORATION (OUT OF GAS?)

PHILIPS

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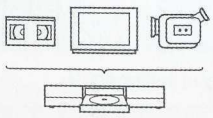

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Letting Buyers Sell Themselves

I HATE BEING SOLD. NEW-PRODUCT PROPAGANDISTS annoy me. Innovation entrepreneurs oozing charisma over their brilliant ideas also fail to persuade. As the poet observed, "A man convinced against his will is of the same opinion still." In other words, while I'm happy to change my mind, I'd really rather change it myself. ▪ That do-it-yourself attitude is at the stubborn heart of a major marketing dilemma for innovators.

Persuading potential customers that your innovation is indispensable is one thing; getting them to persuade themselves of that fact is quite another. This is a critical distinction. Some potential customers desperately want or need to be convinced. In the larger marketplace of novelty and innovation, however, many people prefer the opportunity to convince themselves.

Expanding the question from "How do we persuade people?" to "How do we persuade people to persuade themselves?" poses provocative design choices for innovators. Companies spend appalling amounts of money designing models, prototypes, or simulations that amplify the persuasiveness of their salespeople. But that's a profoundly different task than devising media and methods that empower people to persuade themselves. Precisely because innovators offer the different and the new, they should appreciate that their customers might want to choose how they will be persuaded.

Consider the awkward conversations surrounding retirement planning. Many people are understandably reluctant to discuss the subject for fear of exposing their ignorance or out of concern that they'll be pitched a plethora of "retirement products" from a financial planner working on commission.

Of course, financial-service firms arm their retirement advisors with the latest data and the most sophisticated spreadsheets in an effort to persuade customers to revise their retirement portfolios. Might financial-service firms with innovative offerings be smarter to send those customers very simple spreadsheets that let them see what their retirement income might look like at different savings rates, inflation rates, rates of investment return, and rates of expenditure? These spreadsheets wouldn't be about persuading people to buy; they'd be about giving people the opportunity to play with the possibilities and probabilities for their financial futures. They'd be media for "autopersuasion"—tools with which people could convince themselves that they needed to learn or do more.

The challenge is to get potential customers to play with technologies that reduce their resistance to innovation.

The challenge for innovators is to get potential customers to taste, sample, and play with technologies that reduce their natural—or acquired—resistance to innovation. Let's build on that retirement-planning example. The future is never a simple extrapolation of the present; a truly forward-looking simulation would offer some sort of "Monte Carlo" capacity to survey probabilistic scenarios so people could see how minor shifts in the environment might lead to vastly disparate retirement holdings.

How do you design financial simulations so their users are naturally prompted to test-drive their assumptions using Monte Carlo-like techniques? More provocatively, how does a spreadsheet or any other innovation get you to explore it *without human intervention*, and without forcing users to read pages of esoteric documentation? What a terrific question for Microsoft's Excel group.

In fact, the Wall Street whizzes who develop and sell complex derivatives and "synthetic securities" have already confronted similar design issues. Years ago, these groups treated their "analysis/test" tools as proprietary and wouldn't share them with anyone. Today, however, they give their testing algorithms and analytics to customers. That way, the customers can literally see for themselves how the derivatives and securities they're being asked to purchase will perform under a variety of financial circumstances. As persuasive as the derivatives sales folk may be, the derivatives innovators fully understand that their customers need to be able to convince themselves.

The autopersuasion algorithm is also emerging in the hugely capital-intensive automobile and aerospace markets. Big suppliers now send Boeing, Toyota, and Ford design software and simulations that let them dynamically examine the features of proposed subsystem innovations *before* they're built. Autopersuasion becomes as much a vehicle for risk reduction as a sales tool, and it creates conversations and collaborations between customer and vendor that could never take place otherwise.

As consumers of innovation become ever more sophisticated, the demand for the innovative autopersuasive approach is sure to rise. You're welcome to disagree with this perspective, of course. But please don't try to convince me I'm wrong; give me something to convince myself you're right.

Michael Schrage is codirector of the MIT Media Laboratory's eMarkets Initiative.

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A prototype dashboard camera watches for the heavy blinks of drowsy drivers.

Building a Safer Driver

Technologies that watch for veering, tailgating, and dozing are nearing showrooms

BY PETER DIZIKES

Air bags notwithstanding, auto safety is stuck in neutral. Compared to their huge drop between the mid-1960s and early 1990s, fatality rates have hardly changed in the last decade *(see "Safety Slowdown," facing page)*, and the raw numbers remain appalling: 42,815 people died on U.S. roads last year, 619 more than in 2001. To improve that safety record, some manufacturers plan to install more-sophisticated driver-warning systems, including radar- and video-based safety devices that sense when you veer over lane markings or too close to other cars—and warn you before it's too late.

Unlike previous safety improvements—such as air bags or antilock brakes—which increase the car's ability to protect drivers and passengers from accidents, these new technologies are intended to help avoid accidents in the first place, by giving drivers better information. "We're moving into a new era," says Vicki Neale, a human-factors engineer at Virginia Tech's Transportation Institute. Instead of mechanical systems or devices to protect the car, she says, "the next stages of improvement are going to involve the driver."

To be sure, manufacturers have long considered such devices. Clarence Ditlow, executive director of the Center for Auto Safety, a leading watchdog group in Washington, DC, says such technologies have been prototyped since at least the 1970s but were never implemented—partly because of cost, and partly because there has never been a federal requirement similar to the ones that forced the installation of seat belts and air bags. "Clearly, some of them could have been implemented and should have been implemented," he says. "The industry is not likely to implement them on their own."

COURTESY OF BMW

But that industry posture may be changing. The costs of underlying technologies, from tiny video cameras to microchips, have plummeted. In addition to adding safety, such features could add marketing allure without adding enormous expense for automakers. In the next few years it is likely that these new safety systems, such as lane guidance devices and blind-spot warnings, will actually trickle into showrooms even without new federal requirements.

Automakers including Honda, DaimlerChrysler, Ford, General Motors, and Nissan are all developing lane guidance systems intended to help drivers steer reliably and safely. Using video cameras mounted above rearview mirrors and linked to image-processing software, such systems calculate an auto's relationship to its lane boundaries by tracking painted lane markings on the roadway. As drivers drift, they can be warned by means of dashboard lights, sounds, or seat vibrations. The systems are already nearing deployment; Ford, for example, plans to road-test video sensors on more than 100 vehicles in the next year.

Beyond lane tracking, some systems are designed to increase driver awareness of surrounding vehicles. Volvo says it hopes to introduce a blind-spot warning system within several years. The system starts with backward-facing video cameras mounted on side mirrors. When a driver hits the turn signal with another vehicle in close range, an alarm sounds. "If you can educate drivers about the need to be attentive, and do it by these devices, you can improve driver behavior," says James Sayer, a research engineer at the University of Michigan's Transportation Research Institute.

Other technologies will simply keep drivers' attention focused on the road. GM has introduced a device on the Saab 9.3 that collects data from sources such as the speedometer and even windshield wipers to determine when dashboard messages are appropriate, so that, for example, drivers braking on sharp curves in the rain won't be distracted by nonessential information such as a low-fuel warning light. Beyond suppressing dashboard lights, DaimlerChrysler, Ford, and GM are researching systems that could prevent embedded cell phones from ringing or halt in-car entertainment during stressful driving situations.

The National Highway Transportation Safety Administration plans to road-test lane guidance devices this fall. The agency, which establishes and enforces federal vehicle safety standards, wants to ensure that such systems can compensate for driver errors. Among other things, the agency will assess driver-warning methods such as the dashboard displays, audio signals, and vibrating driver's seats. Although these tests aren't expected to produce federal requirements, they could pave the way for automakers' adoption of these warning devices.

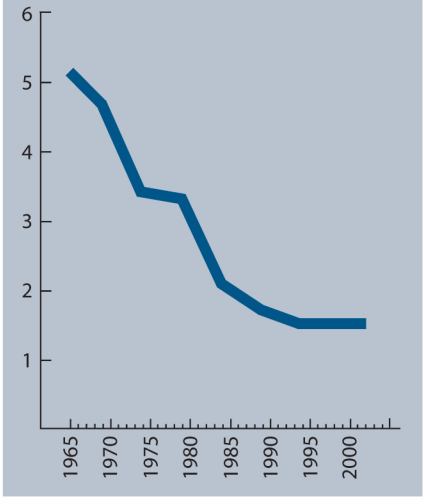
But clearly, automakers face a delicate task. Besides ensuring that new systems don't actually add to distractions, they must craft devices that drivers perceive as helpful high-tech aids, not ego-bruising reprimands. Otherwise, drivers won't want to buy cars that include the new warning systems, industry observers say. "Every driver seems to have the perception that they're better than average," notes Sayer. "Not everybody wants to be told on a regular basis that they are doing something wrong."

In the long term, however, the production of automobiles laden with video and radar sensors could hasten the arrival of passenger vehicles that go beyond warning the driver to actually taking the wheel autonomously, perhaps with the help of a sophisticated road infrastructure.

Although that's still a distant vision, be warned: cars that do their own back-seat driving are closer than they might appear. TR

Safety Slowdown

The rate of fatal U.S. crashes hasn't much improved in a decade. Below, deaths per 160 million vehicle kilometers traveled.



SMART CARS REV UP: A SAMPLING

MANUFACTURER	TECHNOLOGY	EARLIEST COMMERCIALIZATION
Ford (Dearborn, MI)	Video sensors that detect objects in a driver's blind spot during turns and trigger warnings	2006
DaimlerChrysler (Stuttgart, Germany)	Radar-assisted cruise control that maintains separation from other cars at low speeds (devices for highway speeds are already in some cars)	2006
DaimlerChrysler, Ford, Honda (Tokyo, Japan), **Nissan** (Tokyo, Japan)	Video sensors that track lane position and warn drivers against drifting into other lanes	2007
BMW (Munich, Germany)	Camera that tracks eyelid movements and triggers an alarm to alert drowsy drivers	2008
DaimlerChrysler, Ford, GM (Detroit, MI)	Data flow computer that tracks high-stress driving actions and blocks nonessential information	2008

SOURCE: NATIONAL HIGHWAY TRAFFIC SAFETY ADMINISTRATION (SAFETY SLOWDOWN)

ENERGY

Cleaning Up Coal

Today's coal-burning power plants are among the dirtiest sources of fossil fuel power. Gasification power plants—huge pressure cookers that convert coal into a stew of superheated gases that power a turbine—release fewer pollutants than conventional coal plants but still emit vast amounts of carbon dioxide, the leading cause of global warming. Research on cheap carbon dioxide removal, though, is gathering steam—and could make coal gasification a nearly zero-emission fossil fuel power source.

This ceramic membrane blocks carbon dioxide but lets hydrogen through.

Research funded by the U.S. Department of Energy and a consortium of companies, including ChevronTexaco, British Petroleum (BP), and Royal Dutch/Shell, is yielding one of the most promising methods for improving coal gasification: metal-ceramic membranes that only allow hydrogen to pass through, effectively trapping carbon dioxide. The compressed carbon dioxide gas can then be piped off to underground repositories or other permanent storage sites.

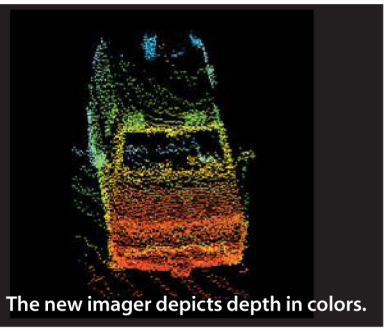
Anthony Sammells, president of Eltron Research—the Boulder, CO, company that developed the technology—says the membranes are 10 times more efficient than competing experimental membranes. That means the membranes approach the efficiency levels needed for commercialization of the technology, says Gary J. Stiegel, the gasification technologies program manager at the Department of Energy's National Energy Technology Lab in Pittsburgh. By September 2004, Eltron Research hopes to move its membrane testing from lab-scale devices to pilot-scale reactors.

If the tests succeed, coal gasification plants could emerge as the cheapest ultralow-emission fossil fuel power plants, trouncing oil or gas plants that use scrubbers and pressurizers to remove carbon dioxide, says Cliff Lowe, an engineer with ChevronTexaco in Richmond, CA.

Indeed, this would make gasification "the technology of choice for coal," says Dale Heydlauff, a senior vice president at a leading coal plant operator, American Electric Power in Columbus, OH. That would help coal overcome its dirty reputation and become a clean power source in the decades to come. —*Peter Fairley*

KEY PLAYERS IN COAL GASIFICATION R&D

COMPANY/AGENCY	TECHNOLOGY EFFORT
U.S. Department of Energy (Washington, DC)	$1 billion, 10-year program to build FutureGen, a nearly emission-free coal gasification power plant
Oak Ridge National Laboratory (Oak Ridge, TN)	Low-cost nanoporous membranes to separate hydrogen and carbon dioxide in gasification plants
Clean Coal Power R&D (Tokyo, Japan)	Low-cost, air-fired coal gasification demonstration plant scheduled for construction in 2004
Nexant (San Francisco, CA) **Simtechе** (Redding, CA) **Los Alamos National Laboratory** (Los Alamos, NM)	Pilot plant to be built by 2005 to capture high-pressure carbon dioxide in solid form from coal gasification
EnCana (Calgary, Alberta) **Dakota Gasification** (Bismarck, ND)	Use of oil fields to store carbon dioxide from coal gasification



The new imager depicts depth in colors.

VISION SYSTEMS

3-D Sky Eye

Military jets need it now. Robots and cars will need something similar in the future: a rugged "vision" system that can produce sharp 3-D images of terrain contours and objects, day or night. This summer, researchers at MIT's Lincoln Laboratory in Lexington, MA, made the first test flights of a 3-D laser imager that can do precisely that.

The new technology uses extremely fast infrared lasers and unique arrays of ultrasensitive light detectors. The laser-emitted light reflects off of objects, and the time it takes to return is measured by detectors, providing a 3-D image. The arrays capture 10,000 images per second and can detect even one photon, says Rick Heinrichs, physicist and group leader at Lincoln Laboratory.

That improves on existing 3-D laser imagers, which scan across a target and more slowly piece together an image, which limits resolution and the ability to visualize partly obscured objects through foliage, for example. What's more, the new arrays "don't have moving parts, making them ultimately cheaper and more reliable," says Maris Juberts, an electrical engineer at the National Institute of Standards and Technology in Gaithersburg, MD.

Of course, "it's going to be a while before this goes to Detroit, because the costs have to go down," says Heinrichs. But already, the airborne version of the imager is seeing the targets through the trees. —*David Talbot*

COURTESY OF ELTRON RESEARCH (COAL); COURTESY OF LINCOLN LABORATORY (EYE)

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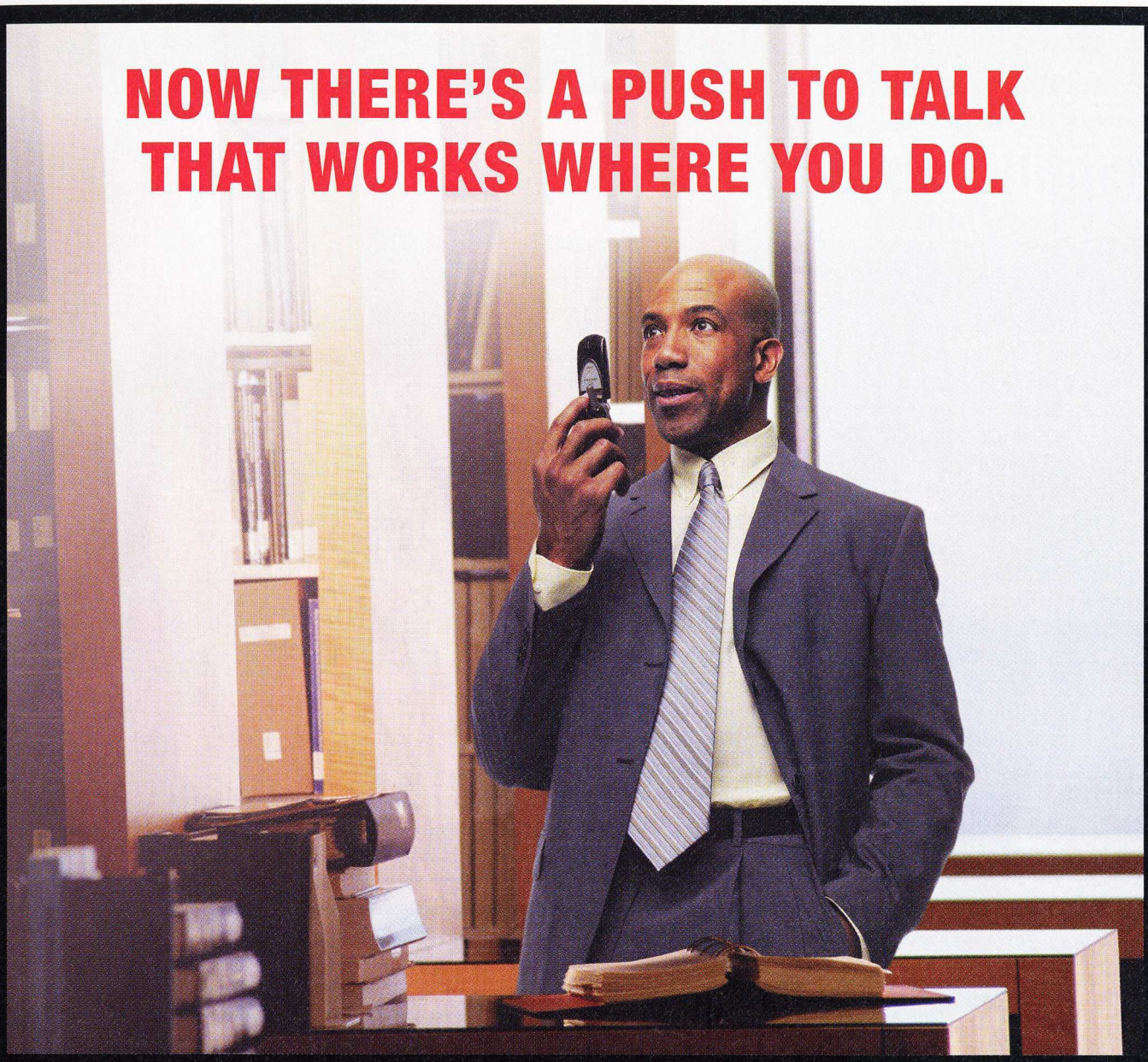

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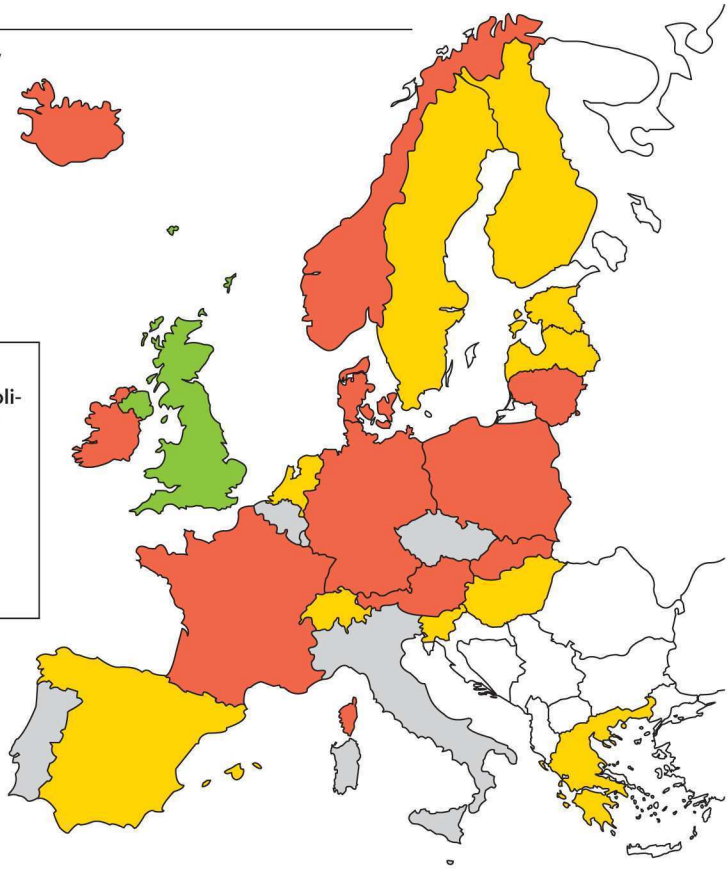
BIOTECH

Mapping a Stem Cell Policy

Embryonic stem cells, with their unique power to differentiate into every type of cell in the human body, have been hailed as the source of possible cures for everything from heart disease to Parkinson's but reviled by antiabortion activists, who oppose harvesting the cells from surplus frozen embryos. When the U.S. government decided in 2001 to deny funding for research that uses embryonic cells derived after August 9, 2001, observers predicted a brain drain of U.S. researchers to Europe.

But European countries are adopting their own restrictions, in some cases tougher than those in the U.S. The resulting patchwork—combined with low biotechnology funding—has hamstrung European embryonic-stem-cell research, says Martyn Postle, director of Cambridge Healthcare and Biotech, a consultancy in Cambridge, England. Worse, he adds, is legislation in the European Parliament—the lawmaking body of the European Union (which includes most European countries; nonmembers include Norway, Switzerland, and Iceland) that could outlaw all embryonic-stem-cell research in the EU. Such a ban would have to be enforced separately in each country. In short, the European research climate is not universally favorable. —*Erika Jonietz*



NOTE: NORWEGIAN RESTRICTIONS ARE PENDING. SOME DATA REFLECT STATUS AS OF APRIL 2003.

WIRELESS

Tracking's New Standard

In the past two years, radio frequency identification tags—silicon chips that carry ID numbers that can be read by computerized radio scanners—have become cheap and tiny enough that such retail behemoths as Wal-Mart are implementing them to track cases of products from warehouses to stores. But makers of these tags aren't keeping good track of each other, making different kinds of tags and readers that aren't all compatible, slowing their widespread adoption.

The tags' communication woes could soon end, however. This fall the Auto-ID Center, an international corporate and university consortium headquartered at MIT, will announce the first hardware and software standards for such tags and their readers. These standards should greatly facilitate the use of the tags by, for example, allowing one reader to be used with different tags. In turn, says David Brock, codirector of the Auto-ID Center, wider adoption of the tags should slash costs from spoilage, theft, and miscounts. "It will be a revolution in the supply chain," he says. "You can see where your items are at any time."

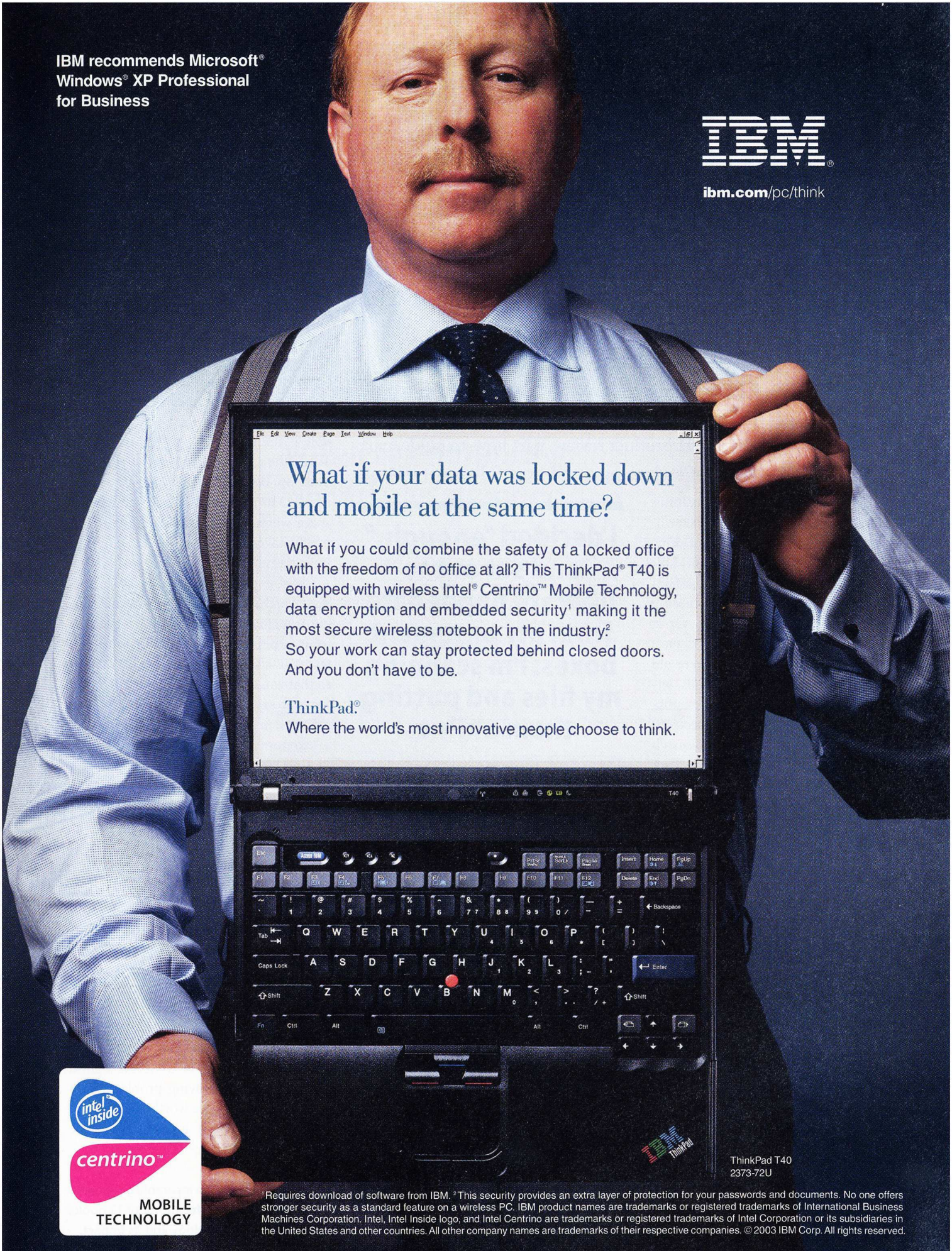
In preparation for the new standards, companies are gearing up to produce readers and tags—which range in size from postage stamps to postcards, and cost as little as 10 cents apiece. Earlier this year, Alien Technology in Morgan Hill, CA, announced that Gillette would buy 500 million tags. And this summer, Wal-Mart—the world's largest retailer—announced it is requiring 100 suppliers to put tags on all pallets of merchandise by 2005. With stores like the Gap, Target, Home Depot, and U.K.-based Tesco and Marks and Spencer making trial runs, radio tags are ready to make tracks. —*Gregory T. Huang*

PLAYERS IN RADIO FREQUENCY IDENTIFICATION

COMPANY	TECHNOLOGY/STRATEGY
Alien Technology (Morgan Hill, CA)	Cheap, mass-produced tags; 500 million sold to Gillette
Matrics (Columbia, MD)	Fast, reliable tags and readers for high-volume tracking; used in supply chains for consumer goods
Royal Philips Electronics (Eindhoven, the Netherlands)	Tags used at the European retailer Metro Group
ThingMagic (Cambridge, MA)	Universal tag readers

The brains of retail radio tags are silicon chips (left) just 350 micrometers wide.

COURTESY OF ALIEN TECHNOLOGY (TRACKING); JOHN MACNEILL (MAP); SOURCES: EUROPEAN UNION RESEARCH COMMISSION AND SWISS AND ICELANDIC GOVERNMENT OFFICES



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Slaying the Paper Dragon

THIS MONTH MARKS THE START OF MY NEW COLumn about digital life. Most of *Technology Review* focuses on the companies and people driving innovation, and how those innovations will affect the world. But here, I'll explore how technology can be incorporated into daily lives. This column will be part product review, part how-to guide, part reflection on the impact of technology, and hopefully a lot of fun. (Readers can find my "Net Effect" column every month on technologyreview.com.)

One of my big projects this past summer was cleaning out the basement. Like many people's, I suspect, my basement was filled with file boxes containing important documents and papers. Or at least, documents and papers that I once thought were important. There were old bank statements and telephone bills, letters my mother sent me at summer camp, my daughter's kindergarten art projects. As a writer, I had also saved research materials collected over a decade's work on books and magazine articles.

It's an old observation that the digital revolution has paradoxically flooded us with paper. But I finally decided that I had had enough and set about to liberate the data from all those dead tree shavings.

So I'm scanning those papers and putting many of them on the Internet. Two things pushed me into action. One is guilt: I have accumulated many paper files on the theory that they might be useful to somebody, someday. But as long as these documents are trapped in my basement, nobody knows they exist. The other is that the technology for turning printed matter into digital has become powerful enough and easy enough to use that I felt I had no excuse not to give it a shot.

The first part of my task—the scanning—hasn't been that hard. My Hewlett-Packard printer/scanner/fax/copier takes a stack of paper and automatically scans its content into Adobe Acrobat files. (To be honest, I only scanned the first hundred pages; then I hired a high-school student to do the rest.) It was then simple to put the files online using standard Web publishing tools.

I decided "enough," and set out to liberate paper data from my basement boxes: I'm scanning my files and putting them online.

But the problem with these scans is they're just pictures of the original documents. They look great, but Google—which searches the Internet for words and phrases—will never index them. Although I could use optical character recognition software to convert the images into searchable text, that would take a lot of time and introduce errors. Instead, I have written a few words to describe each document—something like "Social Security Report, *Privacy Journal*, 2000"—and then put those words and a link to the scanned document on my Web site. Only about a thousand people have downloaded that scan so far. Still, that's a thousand people who probably wouldn't have gotten that report at all otherwise.

Other stuff is not for public consumption, so I'm storing those files securely on my server. Two years ago I bought a digital camera and a copy stand with floodlights on the side and a camera bracket. Since then, I've been photographing my daughter's creations rather than archiving them downstairs. Three drawers of paper artwork have now been captured in 100 digital photographs.

I'm not alone in creating a vast personal digital archive. A friend in Colorado is digitizing his 35-millimeter slides with a slide scanner he bought on eBay; I have dibs on the scanner when he finishes.

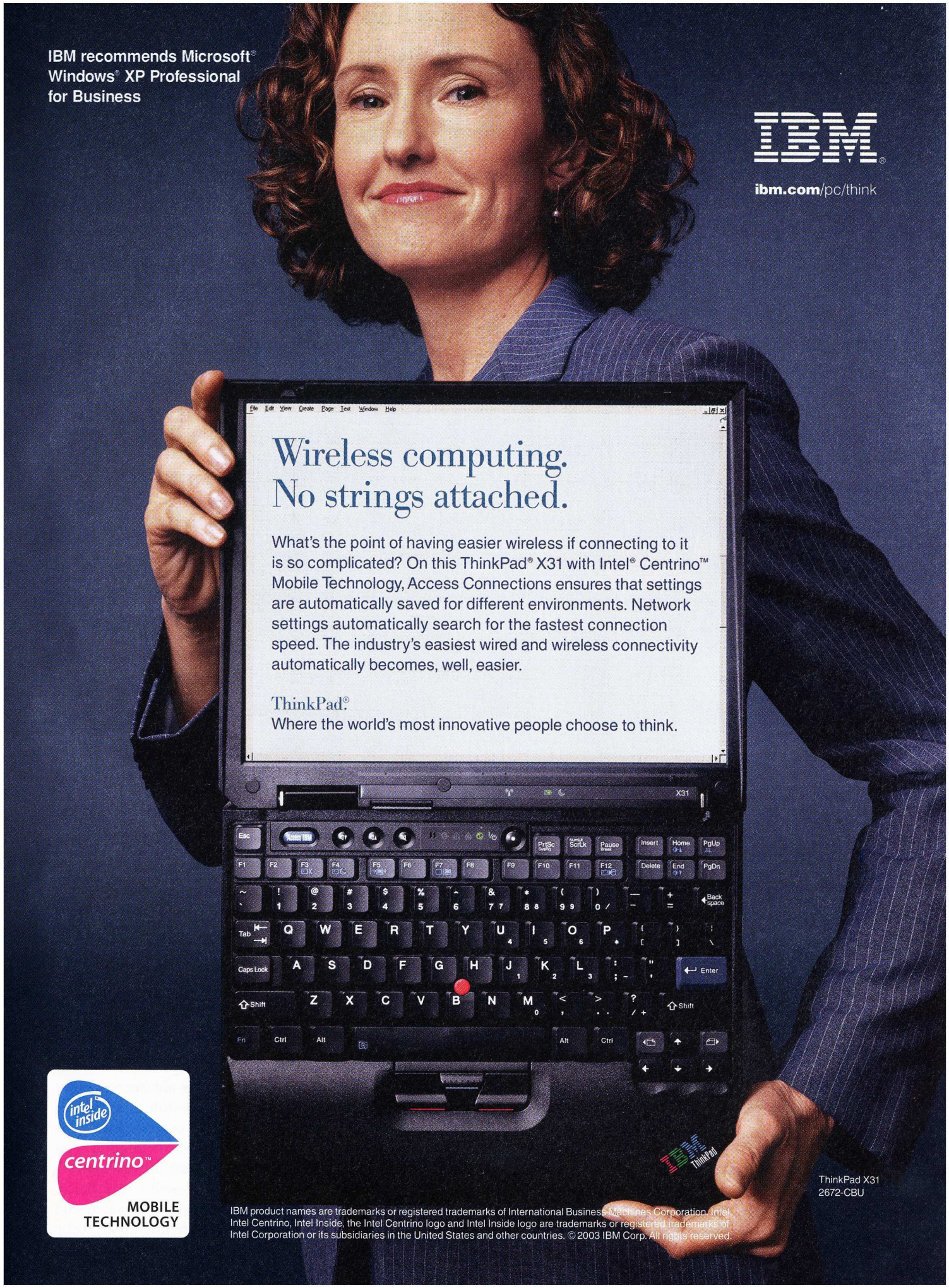
What's making these archives possible is the huge capacity of today's disk drives: the scans of the reference materials from my book *Database Nation* take up nearly 300 megabytes. That was a lot of space when I wrote it back in 1999, but my digital camera today has more storage in its flash memory card.

But if you start creating your own digital archive, you'll discover that digitizing information and entering keywords for Internet search engines is only half the task. You also have to organize digital files so that you can find what you've archived years from now. This complicated job requires, in addition to making backups, a taxonomy that allows you to enlarge and extend your database over decades. Yet another problem, for those making information public, is securing permission from copyright holders to put the data online. You can buy specialty software that fulfills many of these tasks. Unfortunately, these programs store data in proprietary formats. Since I hope to keep my data for 40 or 50 years, that constraint is bound to create hassles down the road: who knows what formats will be supported by systems then in use?

Clearly, this paper escape is still too cumbersome for most people. But if you have both a lot of knowledge about computers and a willingness to devote a good chunk of time to solving problems, you will find the challenge worth tackling.

Now, if I could just digitize those boxes of clothes in my basement.

Simson Garfinkel is an incurable gadgeteer, an entrepreneur, and the author of 12 books on information technology and its impact.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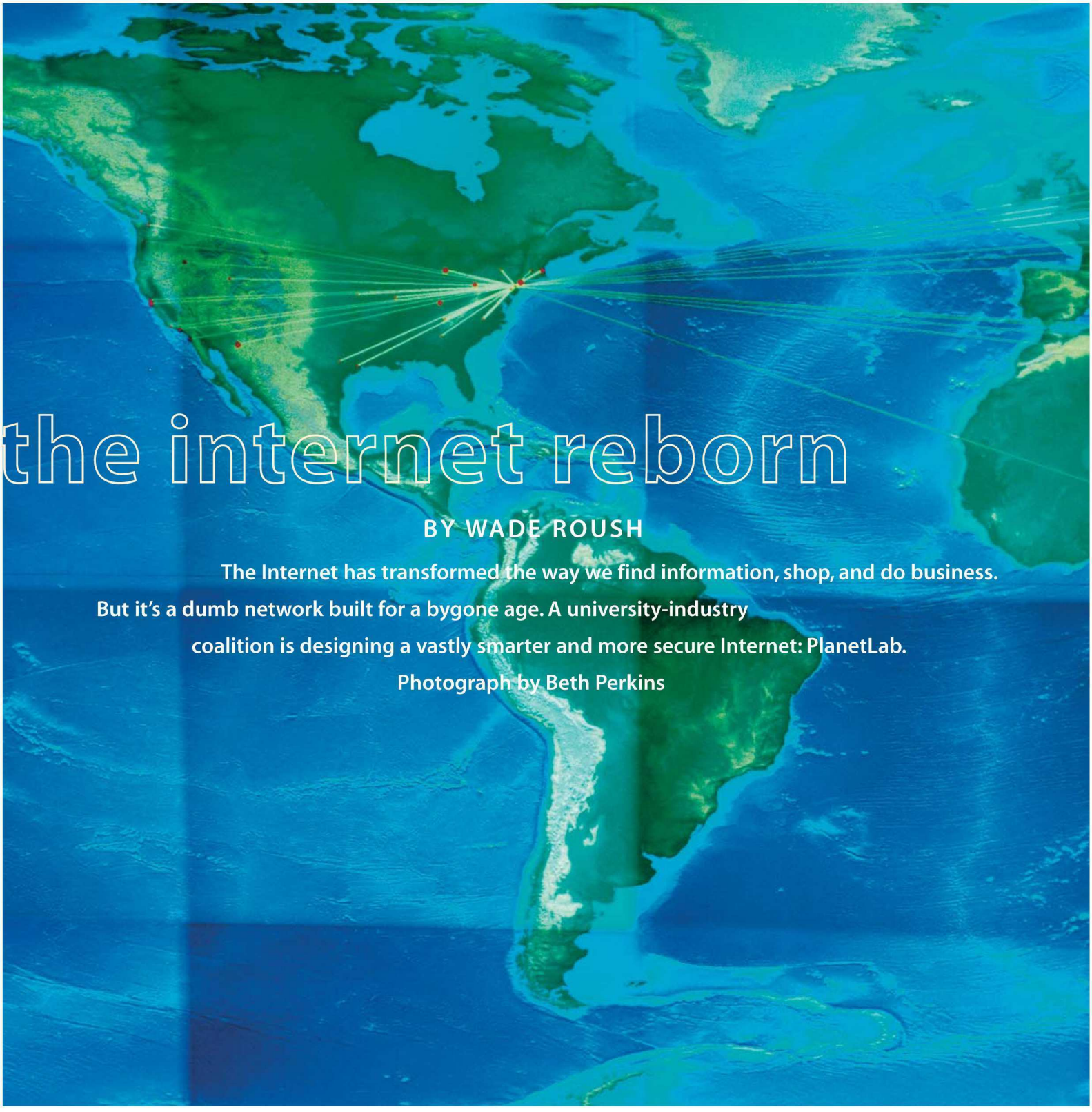


the internet reborn

BY WADE ROUSH

The Internet has transformed the way we find information, shop, and do business. But it's a dumb network built for a bygone age. A university-industry coalition is designing a vastly smarter and more secure Internet: PlanetLab.

Photograph by Beth Perkins

If you're like most cyber-citizens, you use the Internet for e-mail, Web searching, chatting with friends, music downloads, and buying books and gifts. More than 600 million people use these services worldwide—far more than anyone could have predicted in the 1970s, when the Internet's key components were conceived. An estimated $3.9 trillion in business transactions will take place over the Internet in 2003, and the medium's reach is increasingly global: an astonishing 24 percent of Brazilians, 30 percent of Chinese, and 72 percent of Americans now go online at least once per month.

Still, despite its enormous impact, today's Internet is like a 1973 Buick refitted with air bags and emissions controls. Its decades-old infrastructure has been rigged out with the Web and all it enables (like e-commerce), plus technologies such as streaming media, peer-to-peer file sharing, and video-conferencing; but it's still a 1973 Buick. Now, a grass-roots group of nearly 100 leading computer scientists, backed by

Global ambitions: Princeton University's Larry Peterson wants to make the Internet's infrastructure more intelligent.

heavyweight industrial sponsors, is working on replacing it with a new, vastly smarter model.

The project is called PlanetLab, and within the next three years, researchers say, it will help revitalize the Internet, eventually enabling you to

- forget about hauling your laptop around. No matter where you go, you'll be able to instantly recreate your entire private computer workspace, program for program and document for document, on any Internet terminal;
- escape the disruption caused by Internet worms and viruses—which inflicted an average of $81,000 in repair costs per company per incident in 2002—because the network itself will detect and crush rogue data packets before they get a chance to spread to your office or home;
- instantly retrieve video and other bandwidth-hogging data, no matter how many other users are competing for the same resources;
- archive your tax returns, digital photographs, family videos, and all your other data across the Internet itself, securely and indestructibly, for decades, making hard disks and recordable CDs seem as quaint as 78 RPM records.

These predicted PlanetLab innovations—with the potential to revolution-

ize home computing, e-commerce, and corporate information technology practices—can't be incorporated into the existing Net; that would be too disruptive. Instead, the PlanetLab researchers, who hail from Princeton, MIT, the University of California, Berkeley, and more than 50 other institutions, are building their network *on top of* the Internet. But their new machines—called smart nodes—will vastly increase its processing power and data storage capability, an idea that has quickly gained support from the National Science Foundation and industry players such as Intel, Hewlett-Packard, and Google.

Since starting out in March 2002, PlanetLab has linked 175 smart nodes at 79 sites in 13 countries, with plans to reach 1,000 nodes by 2006. It's the newest and hottest of several large-scale research efforts that have sought to address the Internet's limitations *(see "The Internet's Reinventions," p. 36)*. "The Internet has reached a plateau in terms of what it can do," says Larry Peterson, a Princeton computer scientist and the effort's leader. "The right thing to do is to start over at another level. That's the idea behind PlanetLab."

The Network *Is* the Computer, Finally

Like many revolutions, PlanetLab is based on a startlingly simple idea that has been around for a long time, advanced most notably by Sun Microsystems: move data and computation from desktop computers and individual mainframes into the network itself.

But this can't be done with today's Internet, which consists of basic machines, called routers, following 1970s-era procedures for breaking e-mail attachments, Web pages, and other electronic files into individually addressed packets and forwarding them to other machines. Beyond this function, the routers are dumb and inflexible: they weren't designed to handle the level of computing needed to, say, recognize and respond to virus attacks or bottlenecks elsewhere in the network.

PlanetLab's smart nodes, on the other hand, are standard PCs capable of running custom software uploaded by users. Copies of a single program can run simultaneously on many nodes around the world. Each node is plugged directly into a traditional router, so it can exchange data with other nodes over the existing Net. (For that reason, computer scientists call PlanetLab an "overlay" network.) To manage all this, each node runs software that divides the machine's resources—such as hard-drive space and processing power—among PlanetLab's many users *(see "Planetary Pie," this page)*. If the Internet is a global, electronic nervous system, then PlanetLab is finally giving it brains.

The payoff should be huge. Smarter networks will foster a new generation of distributed software programs that preempt congestion, spread out critical data, and keep the Internet secure, even as they make computer communications faster and more reliable in general. By expanding the network as quickly as possible, says Peterson, the PlanetLab researchers hope to restore the sense of risk-taking and experimentation that ruled the Internet's early days. But Peterson admits that progress won't come easily. "How do you get an innovative service out across a thousand machines and test it out?"

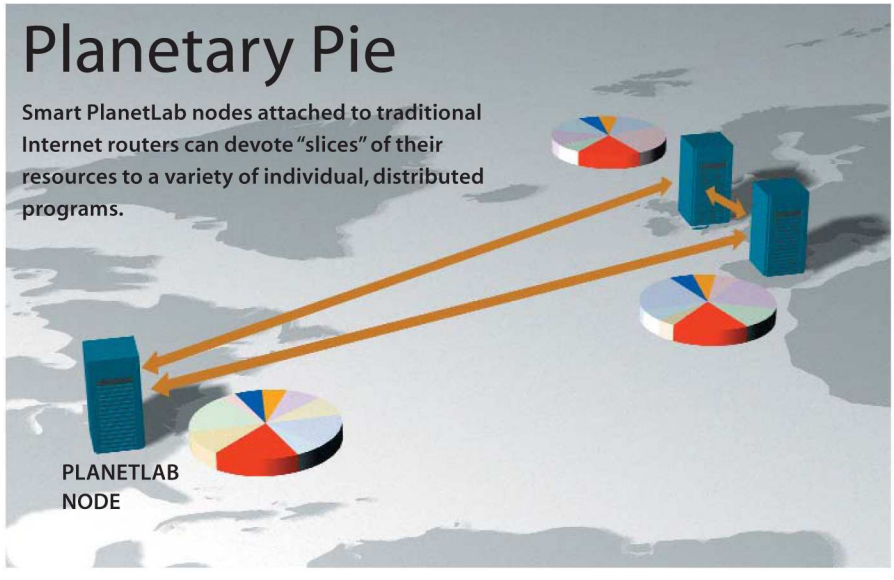
It helps that the network is no longer just a research sandbox, as the original Internet was during its development; instead, it's a place to deploy services that any programmer can use and help improve. And one of the Internet's original architects sees this as a tremendously exciting trait. "It's 2003, 30 years after the Internet was invented," says Vinton Cerf, who codeveloped the Internet's basic communications protocols as a Stanford University researcher in the early 1970s and is now senior vice president for architecture and technology at MCI. "We have millions of people out there who are interested in and capable of doing experimental development." Which means it shouldn't take long to replace that Buick.

Baiting Worms

The Achilles' heel of today's Internet is that it's a system built on trust. Designed into the Net is the assumption that users at the network's endpoints know and trust one another; after all, the early Internet was a tool mainly for a few hundred government and university researchers. It delivers packets whether they are legitimate or the electronic equivalent of letter bombs. Now that the Internet has exploded into the cultural mainstream, that assumption is clearly outdated: the result is a stream of worms, viruses, and inadvertent errors that can cascade into economically devastating Internet-wide slowdowns and disruptions.

Take the Code Red Internet worm, which surfaced on July 12, 2001. It quickly spread to 360,000 machines around the world, hijacking them in an attempt to flood the White House Web site with meaningless data—a so-called denial-of-service attack that chokes off legitimate communication. Cleaning up the infected machines took system administrators months and cost businesses more than $2.6 billion, according to Computer Economics, an independent research organization in Carlsbad, CA.

Thanks to one PlanetLab project, Netbait, that kind of scenario could



JOHN MACNEILL

Netbait

BRENT CHUN, INTEL

▶ A Defense Early Warning line for computer worms, using PlanetLab nodes around the world as its eyes and ears.

EMILY NATHAN

become a thing of the past. Machines infected with Code Red and other worms and viruses often send out "probe" packets as they search for more unprotected systems to infect. Dumb routers pass along these packets, and no one is the wiser until the real invasion arrives and local systems start shutting down. But in theory, the right program running on smart routers could intercept the probes, register where they're coming from, and help administrators track—and perhaps preempt—a networkwide infection. That's exactly what Netbait, developed by researchers at Intel and UC Berkeley, is designed to do.

This spring, the program showed how it can map a spreading epidemic. Brent Chun, Netbait's author, is one of several senior researchers assigned to PlanetLab by Intel, which helped launch the network by donating the hardware for its first 100 nodes. Chun ran Netbait on 90 nodes for several months earlier this year. In mid-March, it detected a sixfold spike in Code Red probes, from about 200 probes per day to more than 1,200—a level of sensitivity far beyond that of a lone, standard router. The data collected by Netbait showed that a variant of Code Red had begun to displace its older cousin.

As it turned out, there was little threat. The variant turned out to be no more malignant than its predecessor, for which remedies are now well known. But the larger point had been made. Without a global platform like PlanetLab as a vantage point, the spread of a new Code Red strain could have gone undetected until much later, when the administrators of local systems compared notes. By then, any response required would have been far more costly.

Netbait means "we can detect patterns and warn the local system administrators that certain machines are infected at their site," says Peterson. "That's something that people hadn't thought about before." By issuing alerts as soon as it detects probe packets, Netbait could even act as an early-warning system for the entire Internet.

Netbait could be running full time on PlanetLab by year's end, according to Chun. "Assuming people deem the service to be useful, eventually it will get on the radar of people at various companies," he says. It would then be easy, says Chun, to offer commercial Internet service providers subscriptions to Netbait, or to license the software to companies with their own planetwide computing infrastructures, such as IBM, Intel, or Akamai.

Traffic Managers

Just as the Internet's architects didn't anticipate the need to defend against armies of hackers, they never foresaw flash crowds. These are throngs of users visiting a Web site simultaneously, overloading the network, the site's server, or both. (The most famous flash crowd, perhaps, formed during a 1999 Victoria's Secret lingerie Web broadcast that had been promoted during the Super Bowl. Within hours, viewers made 1.5 million requests to the company's servers. Most never got through.) Such events—or their more malevolent cousins, denial-of-service attacks—can knock out sites that aren't protected by a network like Akamai's, which caches copies of customers' Web sites on its own, widely scattered private servers. But the question is how many copies to make. Too few, and the overloads persist; too many, and the servers are choked with surplus copies. One solution, described in papers published in 1999 by the researchers who went on to found Akamai, is simply to set a fixed number.

In the not-too-distant future, PlanetLab nodes will adjust the number of cached copies on the fly. Here's how it works. Each node devotes a slice of its processor time and memory to a program designed by Vivek Pai, a colleague of Peterson's in the computer science department at Princeton. The software monitors requests for page downloads and, if it detects that a page is in high demand, copies it to the node's hard drive, which acts like the memory in a typical Web server. As demand grows, the program automatically caches the page on additional nodes to spread out the load, constantly adjusting the number of replicas according to the page's popularity. Pai says that simulations of a denial-of-service attack on a PlanetLab-like network showed that nodes equipped with the Princeton software absorbed twice as many page requests before failing as those running the algorithms published by the Akamai founders.

This new tool, known as CoDeeN, is already running full time on PlanetLab; anyone can use it, simply by changing his or her Web browser's settings to connect to a nearby PlanetLab node. It's a work in progress, so service isn't yet fully reliable. But Pai believes the software can support a network with thousands of nodes, even-

CoDeeN

VIVEK PAI, PRINCETON UNIVERSITY

▶ No more World Wide Wait: CoDeeN automatically moves Web pages closer in the network to the people using them.

tually creating a free "public Akamai." With this tool, Internet users would be able to get faster and more reliable access to any Web site they chose.

But banishing flash crowds won't, by itself, solve Internet slowdowns. Other PlanetLab software seeks to attack a subtler problem: the absence of a decent "highway map" of the network. Over the years the Internet has grown into an opaque tangle of routers and backbone links owned by thousands of competing Internet service providers, most of them private businesses. "Packets go in, they come out, and there's very little visibility or control as to what happens in the middle," says Thomas Anderson, a computer scientist at the University of Washington in Seattle.

One solution is software known as Scriptroute. Developed by Anderson and his colleagues at the University of Washington, it's a distributed program that uses smart nodes to launch probes that fan out through particular regions of the Internet and send back data about their travels. The data can be combined into a map of the active links within and between Internet service providers' networks—along with measurements of the time packets take to traverse each link. It's like having an aerial view of an urban freeway system. Anderson says operators at Internet service providers such as AOL and Earthlink, as well as universities, could use Scriptroute's maps to rapidly diagnose and repair network problems in one to three years.

Sea Change

Keeping data intact can be just as tricky as transmitting it: ask anyone who has left a personal digital assistant on a train or suffered a hard-drive crash. What's needed, says Berkeley computer scientist John Kubiatowicz, is a way to spread data around so that we don't have to carry it physically, but so it's always available, invulnerable to loss or destruction, and inaccessible to unauthorized people.

That's the grand vision behind OceanStore, a distributed storage system that's also being tested on PlanetLab. OceanStore encrypts files—whether memos or other documents, financial records, or digital photos, music, or video clips—then breaks them into overlapping fragments. The system continually moves the fragments and replicates them on nodes around the planet. The original file can be reconstituted from just a subset of the fragments, so it's virtually indestructible, even if a number of local nodes fail. PlanetLab nodes currently have enough memory to let a few hundred people store their records on OceanStore, says Kubiatowicz. Eventually, millions of nodes would be required to store everyone's data. Kubiatowicz's goal is to produce software capable of managing 100 trillion files, or 10,000 files for each of 10 billion people.

To keep track of distributed data, OceanStore assigns the fragments of each particular file their own ID code—a very long number called the Globally Unique Identifier. When a file's owner wants to retrieve the file, her computer tells a node running OceanStore to search for the nearest copies of fragments with the right ID and reassemble them.

Privacy and security are built in. An owner who wants to retrieve a file must first present a key that has been generated using now common encryption methods and stored in a password-protected section of her personal computer. This key contains so many digits that it's essentially

Change of Address

Dumb routers aren't the Internet's only limitation. The profusion of devices with Internet connectivity—laptops, handheld devices, appliances, and soon car and aircraft systems and even remote sensors—is creating a shortage of Internet Protocol (IP) addresses. But a coming overhaul of the address system will result in an almost inconceivably vast number of unique digital addresses.

Today, any device that uses the Internet has an address made up of 32 binary digits. This scheme, laid out in the early 1980s, provided for a maximum of about 4.3 billion unique addresses. Turns out, given the proliferation of devices that's on the way, that's not enough. So the coming version of the Internet Protocol, which will be implemented over the next several years, will create codes that have 128 binary digits. A number that long allows so many possible combinations that there will be some 670 quadrillion (thousand trillion) addresses for every square millimeter of Earth's surface—which ought to be enough for a while.

BETH PERKINS

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The Internet's Reinventions

PlanetLab aims to transform today's dumb, simple Internet communications system into a smarter and much more flexible network that can ward off worms, store huge amounts of data with perfect security, and deliver content instantly. Here's how it fits into a long tradition of academic and government research projects that developed fundamental networking, transmission, and distributed-computing technologies.

1969

ARPANET

The first major attempt to use computers for communication, and the testing ground for the standards that would come to define the Internet. Built by universities and technology firms with funding from the U.S. Defense Department's Advanced Research Projects Agency (now DARPA).

1973–1983

The Internet

A network of smaller networks in which computers exchange packets of data formatted and addressed according to, respectively, the Transport Control Protocol and the Internet Protocol (TCP/IP), which were conceived in 1973 and officially replaced the ARPANET's protocols in January 1983.

1992

MBone

The Multicast Backbone: a system that allows many people to view the same real-time information, such as video broadcasts, over the Internet. Created by members of the Internet Engineering Task Force in 1992 to overcome the limitations of standard Internet protocols, which can route a given data packet to only one destination.

1996

Internet2

A consortium of more than 200 universities that has created Abilene, a network of high-performance routers and fiber-optic links. Abilene is able to transmit an entire DVD movie in about 36 seconds, as much as 3,500 times faster than a typical home DSL or cable connection.

The Grid

A collection of public and private organizations and projects that use software developed at the U.S. Department of Energy and the University of Southern California to link scattered supercomputers, scientific instruments, and data storage facilities into a "grid" that can take on tough computational problems—like screening for new drug molecules.

2000

ABone

The Active Network Backbone: a network built to test the efficiency of "active networking," in which the network is stripped of nearly all intelligence—even the basic message-passing software that runs on today's Internet—and packets of data contain all the software and instructions needed to deliver themselves to their destinations. Funded by DARPA and created by SRI International, a private research institute in Menlo Park, CA, and the University of Southern California.

2002

PlanetLab

An effort by academic and corporate networking researchers to augment, and eventually replace, today's "dumb" Internet with a much smarter network able to monitor itself for worms and viruses, relieve bottlenecks automatically, and make personal-computing environments portable to any terminal on earth.

impossible for others to guess it and gain unauthorized access. The key provides access to OceanStore directories that map human-readable names (such as "internet.draft") to fragment ID codes. The ID codes are then used to search OceanStore for the nearest copies of the needed fragments, which are reassembled and decrypted. And there's one more layer of protection: the ID codes are themselves generated from the data's contents at the time the contents are saved using a secure cryptographic function. Like encryption keys, the codes are so long (160 binary digits) that even today's most advanced supercomputers can't guess or fake them. So if data retrieved from OceanStore has an unaltered ID, the owner can be sure the data itself hasn't been changed or corrupted.

Kubiatowicz would like to see OceanStore become a utility similar to DSL or cable Internet service, with consumers paying a monthly access fee. "Say you just got back from a trip and you have a digital camera full of pictures," he suggests. "One option is to put these pictures on your home computer or write them to CDs. Another option is that you put those pictures into OceanStore. You just copy them to a partition of your hard drive, and the data is replicated efficiently on a global scale." That option could be available within three to five years, he predicts, but in the interim, two things need to happen. First, his team needs to produce sturdier versions of the OceanStore code. Second, someone needs to provide enough nodes to enlarge the system to a useful scale. That someone is likely to be a private company looking to enter the distributed-storage business, predicts Peterson. "I could imagine OceanStore attracting the next Hotmail-like startup as its first customer," he says.

Beyond providing distributed, secure storage, OceanStore could eventually make every computer your personal one. At its next level of development, it could store your entire computing environment—your PC desktop, plus all of the applications you're running and all the documents you have open—across the network and reconstitute it on demand, even if you popped up at an Internet termi-

nal halfway around the world. This capability would be useful to the businessperson on the road, to a doctor who suddenly needs to review a chart, or to a contractor who wants to tweak a blueprint from home. Several companies are working to realize this vision. Intel calls it Internet Suspend/Resume, and Sun researchers are testing several approaches to "desktop mobility." But PlanetLab could provide the infrastructure that makes such technology possible, by offering a means to manage the large amounts of data—perhaps tens of gigabytes—that personal-computer users might regularly rely on.

Laundry List

Such ideas may seem radical. Then again, just a decade ago, so did e-commerce. The question now is which big idea will evolve into the Google or Amazon.com of the new, smarter Internet. By charter, PlanetLab can't be used for profit-making enterprises, but businesses may soon spring from the platform it provides. "We want it to be a place where you leave services running long-term—which brings us much closer to the point where someone commercial might want to adopt it or replicate it for profit," Peterson says. That could happen if the experiments running now, along with the methods being developed to keep the network operating smoothly, provide a reliable model for future intelligent networks. "We don't know where that next big idea is going to come from," says Peterson. "Our goal is just to provide the playing field."

PlanetLab's early industry sponsors, such as Intel and Hewlett-Packard, may be among the first to jump in. HP Labs in Palo Alto, CA, for example, installed 30 PlanetLab nodes in June and plans to use the network to road-test technologies that could soon become products. One example: software developed by researcher Susie Wee that uses a CoDeeN-like distribution network to deliver high-resolution streaming video to mobile devices. The goal is to avoid wasting bandwidth, and Wee's software would do just that by streaming, say, video of a major-league baseball game to a single local node, then splitting the data into separate streams optimized for the screen resolutions of different viewers' devices—whether desktop PCs, wireless laptops, PDAs, or cell phones. HP or its licensees could bring such a service to market within two years, Wee says. Projects like this one, says Rick McGeer, HP Labs' scientific liaison to a number of university efforts, means that PlanetLab is "not only a great experimental test bed, it's a place where you can see the demonstrable value of services you don't get on today's Internet."

Of course, researchers' enthusiasm about smart networks doesn't keep them from pondering the new problems they could create. Until now, viruses and worms have always been launched from machines at the Internet's edges; imagine how much more damage an attack could do if it originated from a trusted node inside the network. And there's no centralized authority to force local PlanetLab machines to meet security standards, as there is with Akamai and other private networks. But researchers at Princeton and other PlanetLab member institutions say they're already working on ways to avoid these hazards.

While it's impossible to know which blockbuster new technology and business paradigms will emerge from smarter networks, projects like PlanetLab virtually ensure that the Internet will eventually fulfill some of its long-unrealized potential in areas like broadband access, security, shared storage, and reliable video, text, and other content delivery. "There is a long laundry list of things we can and should do better on the Internet," Internet pioneer Cerf says. "Why didn't we do it before? Well, some of it is that they are hard problems; some of it is because the technology wasn't capable enough—we needed more brute-force computing capability than we had 20 years ago. And in some cases, it's because nobody cared."

That's now changing. Peterson expects that ultimately PlanetLab and similar networks will bring about a wholesale reinvention of the Internet. As smart nodes are installed at more of the Internet's existing hubs, these networks could multiply to the point that they cease to be add-ons at all and simply *become* the next generation's Internet. As Peterson puts it, "This is exactly the Internet all over again." The results could be as different from e-mail and Web browsing as those technologies are from the telephone—or a 1973 Buick is from a low-emissions, fuel-efficient Toyota—with impact to match.

Wade Roush is a *Technology Review* senior editor based in San Francisco.

OceanStore

JOHN KUBIATOWICZ,
UNIVERSITY OF CALIFORNIA, BERKELEY

▶ Who needs disk drives when your data can be broken up, scattered across the Internet, and reassembled at will?

EMILY NATHAN

REVITALIZING DRUG DISCOVERY

Back to the drawing board: Jacky Vonderscher says Novartis is rethinking the way scientists work together.

The pharmaceutical industry's R&D spending is steadily climbing, but the flow of new products from the drug pipeline is slowing to a trickle. Now companies are scrambling to use genomics, proteomics, and the other technologies that have transformed biology to boost the speed and efficiency of drug development.

BY STEPHEN S. HALL • PHOTOGRAPH BY KATHLEEN DOOHER

It was the kind of detail that

pharmaceutical executives at $20 billion companies don't typically bother pointing out. But Jacky Vonderscher, vice president and head of drug development at the Novartis Institutes for Biomedical Research in Cambridge, MA, paused while guiding a visitor through the company's spanking new research labs to sing the praises of...a hallway. True, it was open, airy, and exceptionally commodious, but all the same, it was a hallway, running

through the institute's oncology and infectious-disease research laboratories. No one was likely to discover a new blockbuster drug in this hallway, any more than a scientist was likely to think up a cure for cancer while dreamily staring out the tall windows lining nearby labs.

Or were they?

"You see, it's not just laid out as a square," Vonderscher explained over his shoulder as he hurried along the corridor. Indeed, the hallway sliced through the labs at a provocative angle, revealing office geometry according to Picasso, not Mondrian. That architectural detail is just one small part of the multibillion-dollar attempt Novartis is making to provoke innovation by cutting across departments and disciplines, bringing people together in odd juxtapositions, and knocking down the walls between academic and entrepreneurial interests. In choosing Cambridge as the site of a new $4 billion operation, which will be the company's worldwide research headquarters, "We are trying to think of everything that affects the dynamics of the scientists and their interactions with each other," Vonderscher explained.

Like many other pharmaceutical companies, Novartis is in the midst of trying to revitalize the drug discovery process. Throughout the industry, that process has long followed a standard—and perilous—progression: identify a biological target like an enzyme or a gene that appears related to a disease; fling hundreds of thousands of compounds at the target in the hopes that several of them will interact with it; study the toxicity, absorption, and other physiological properties of the most promising molecules in animals; and if all still looks encouraging, test one of the compounds in humans. The entire marathon can easily take a decade and cost hundreds of millions of dollars. And actually getting across the finish line is particularly brutal: the failure of many potential drugs, for either safety or efficacy reasons, often does not become apparent until large-scale clinical trials involving hundreds of patients, which is why only about one in ten compounds that enter human testing succeeds and becomes a drug.

"When you think that the best people at good companies sit around and make decisions about bringing something into human development, and nine out of ten of those molecules fail—that's amazing," says Bennett M. Shapiro, who in August retired as executive vice president for worldwide licensing and external research at Merck. "So it's obvious that if we can decrease our failure rate from nine to eight, we've doubled the output of our operation as if we had doubled the size of the lab."

The stakes in this game are higher than ever. The pipelines of future products at many pharmaceutical companies emit no more than a trickle of largely prosaic, me-too drugs—copycat cholesterol reducers and mood elevators—just as the patents on pharmaceutical blockbusters such as Zocor and Paxil are about to expire. And despite the industry's steady increase in R&D expenditure, which now totals more than $25 billion annually in the United States alone, U.S. Food and Drug Administration statistics show a steady decline in the approval of "new molecular entities"—drugs whose active ingredients have never before been approved in the United States—since 1996 *(see "Troubling Trends," facing page)*. In part, the decline indicates that much of the low-hanging fruit has been plucked; but it also points to the fact that it takes a number of years for new technologies to be incorporated into the drug discovery process.

To refill the pipeline, and to squeeze that one additional success out of every ten human trials, pharmaceutical compa-

Innovation Outposts

Some of the newest pharmaceutical "lablets" are positioned to take advantage of the latest science and the hottest research communities.

COMPANY	LABLET LOCATION	FOCUS
Pfizer	Cambridge, MA	Ultrafast screening of genome-derived drug targets
Abbott Laboratories	Parsippany, NJ	Autoimmune disease
GlaxoSmithKline	Upper Merion, PA	Cardiovascular and urogenital diseases
	Research Triangle Park, NC	Metabolic and viral diseases
	Upper Providence, PA	Microbial, musculoskeletal, and proliferative diseases
	Harlow, England	Neurology and gastrointestinal conditions
	Verona, Italy	Psychiatry
	Stevenage, England	Respiratory conditions and inflammation

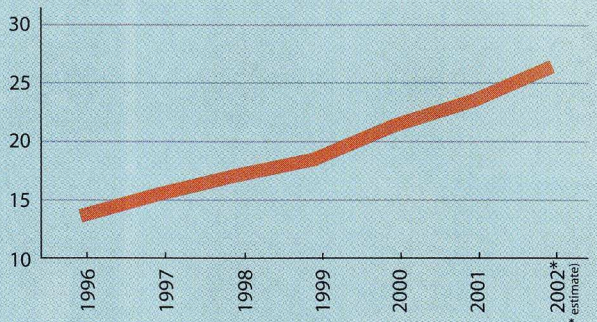
nies have been doing all they can to reap the benefits of the latest advances in molecular biology, changing everything from corporate culture (right down to the hallways running between their labs) to the nature of their collaborations with university researchers. They are seeking to combine the basic fascination of academic biological research with the passion and entrepreneurial zest of biotechnology companies, all coupled to the economic brawn of major corporations. This transition has been under way at many pharmaceutical companies for several years, but firms are now moving rapidly to search out mergers, forge collaborations with academic groups, strike deals with biotechnology companies, and establish outposts near hotbeds of university research. In short, drug companies are positioning themselves—geographically, technologically, and even sociologically—to take full advantage of the gush of information that is revolutionizing biology and medicine.

Researchers in both academia and industry are still digesting the mass of genetic information resulting from the Human Genome Project. Drug industry executives say genomic information and technology have to date had little effect on drug discovery *(see "Feeling the Burn," p. 44)*. But in the long run, a better understanding of the roles genes, proteins, and metabolites such as glucose and fatty acids play in the body does promise a more mechanistic, nuts-and-bolts understanding of diseases. And that increased understanding should, in theory at least, make drug discovery speedier and more efficient—by enabling researchers to identify many more targets, recognize problems with safety and drug metabolism earlier, and shape the design of clinical testing to improve the odds of success.

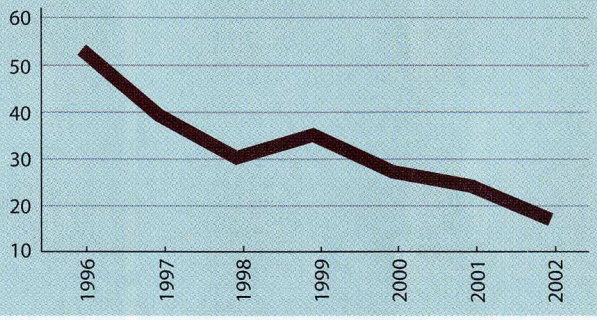
Troubling Trends

The drug industry's R&D spending in the U.S. is climbing, but fewer and fewer wholly new drugs, or "new molecular entities," are winning federal approval and reaching the market.

U.S. R&D (IN BILLIONS OF DOLLARS)



NEW MOLECULAR ENTITIES APPROVED



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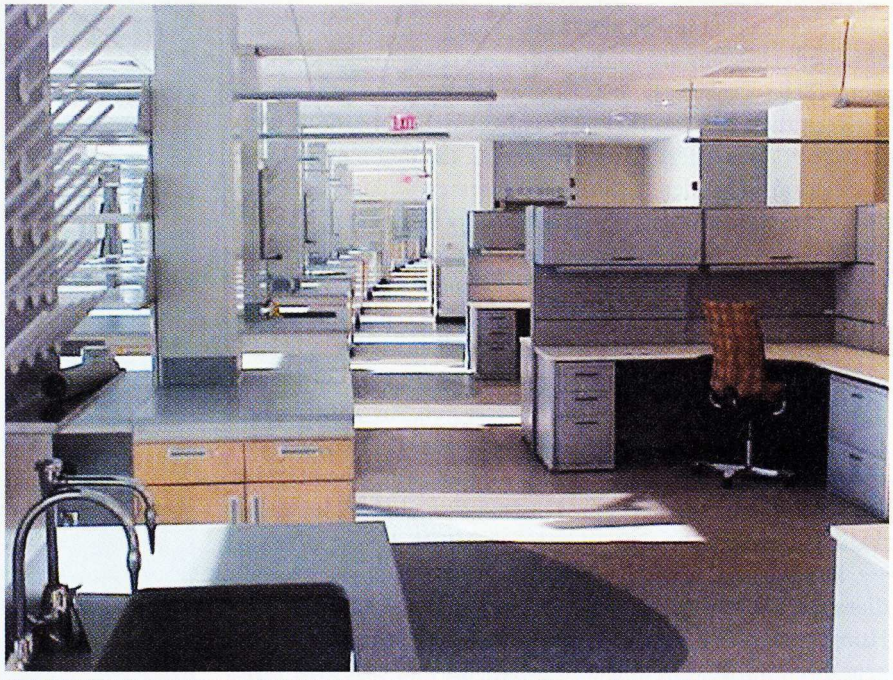
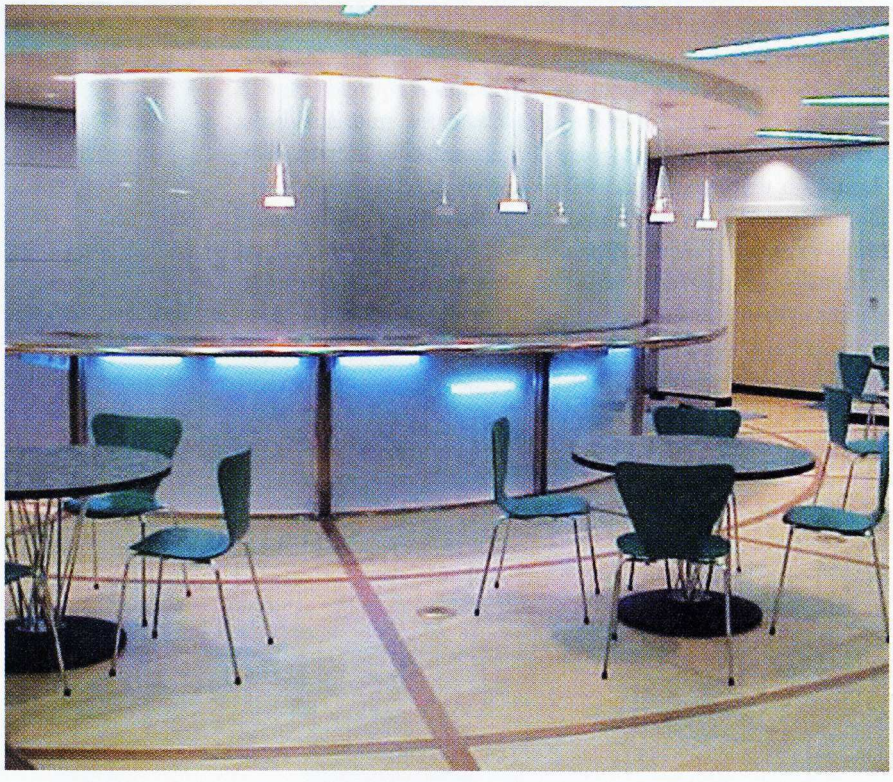




Atmosphere of innovation: Every aspect of the Novartis Institutes for Biomedical Research, from the labs to the break rooms to the hallways, was designed to bring people and ideas together.

COURTESY OF PAUL KRIEGER

The marriage of pharmaceutical companies and the "new biology" is being consummated in a host of different ways. In 2001, Merck acquired the genomics company Rosetta Inpharmatics of Seattle in a stock deal worth $540 million; the deal gives Merck access to Rosetta's technology for looking at which genes are turned on or off by a given drug candidate, an early indication both of the potential efficacy of the compound and of its potential toxicity. GlaxoSmithKline has established six so-called Centers of Excellence for Drug Discovery; each of these centers brings new molecular-biology tools and a small, entrepreneurial ethic to a research mission such as developing treatments for diabetes or cancer. And many companies are hanging out their shingles in research communities such as Cambridge, San Diego, and Seattle, locating satellite labs ("lablets," in current lingo) cheek-to-jowl with major academic and biotech facilities *(see "Innovation Outposts," p. 40).*

An early example of such an outpost is Pfizer's Discovery Technology Center in Cambridge. In 1996, Pfizer established the center and launched its "Drug Pfinder" program, in which academic scientists working in genomic research are encouraged to share discoveries (and, potentially, financial rewards) with Pfizer researchers prior to the publication of their findings. "The idea of the DTC is to focus on gene families" that include a wealth of potential drug targets, says Ching-Hua Tseng, a senior research scientist at the center. "We can para-

Novartis is moving its R&D headquarters from Switzerland to the United States, hoping the gamble will pay off in an approach that allows researchers to be more clever about drug discovery.

chute these projects directly into therapeutic areas," he adds. "The goal is to accelerate drug discovery at other Pfizer sites."

BASIC BIOLOGY

Of all these efforts, perhaps none is being watched as closely as Novartis's. Vonderscher, an Alsatian-born biochemist who trained in Lyon and has been with Novartis (or one of its predecessors, Ciba-Geigy) for nearly 25 years, has a craggy, bearded, Gallic face that seems to be animated by a permanent, if controlled, sense of urgency. What Novartis and other pharmaceutical companies are trying to do right now, he explained, is take a hard look at biotechnology and selectively adopt those technologies "that will help us in boosting our pipeline and our drug discovery processes." It's not a simple task, he said, "because, especially five years ago, there were a lot of interesting things, but there was a lot of crap in the biotech world at the same time." Despite his skepticism about the lack of discipline in the less mature biotech industry, however, Vonderscher stressed that it has much to offer the pharmaceutical industry. "We need the risk-taking of biotechs," he said.

$25 billion plus went to pharmaceutical R&D in the U.S. in 2002.

Indeed, in shifting the heart of its R&D efforts from Basel, Switzerland, to Cambridge, Novartis is in effect abandoning technology roots that stretch back several centuries through its predecessor companies, Sandoz and Ciba-Geigy. The hope is that the multibillion-dollar gamble in making the move will pay off in an approach that will, in Vonderscher's words, allow researchers to be "more clever"—that is, allow the company to identify problems (and possibilities) and make shrewder decisions earlier in the drug discovery process. Part of that added cleverness derives from new technologies based on an increased understanding of biology, and part from a change in corporate culture.

The culture of drug discovery at Novartis began to change in 2002, when the company hired Mark C. Fishman, head of cardiology at Massachusetts General Hospital and a professor at Harvard Medical School, to lead all of its research and devel-

opment efforts. Fishman is a respected cardiologist who also brings blue-ribbon credentials as a basic researcher studying the genetic and molecular mechanisms of cardiac development. He immediately instilled the ethic that a more academic-style understanding of biological processes and pathways could speed up the drug discovery process—even though basic research is often viewed as slow, tedious, and curiosity-driven rather than market-driven.

Key to Novartis's new enterprise is a shift from focusing on particular molecules as targets to looking at biological pathways—interconnected sequences of biological events that together affect the course of a disease. Teasing apart biological pathways used to be a purely academic pursuit, and it can be a laborious and time-consuming process, but Novartis believes that the new molecular-biology tools will sharpen the understanding of the pathways and increase the odds of making unexpected discoveries. "I call it guided serendipity," said Vonderscher.

Novartis has paid a great deal of attention to creating an infrastructure for this guided serendipity, and has done so very rapidly. "This was an empty shell in the summer of 2002," Vonderscher said, walking through the lobby of the new research headquarters in Cambridge. Although there was a hectic, unsettled feel to the place—Vonderscher's office still had boxes waiting to be unpacked, and many labs remained vacant—the research and development staffs were rapidly ramping up; every other Monday morning, management circulated a list of another ten or so new employees. The facility is slated to house a total of about 400 researchers by the end of the year.

MAKING DEALS

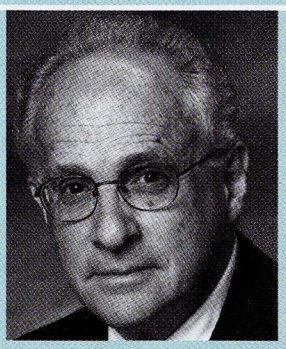
Creating new, centralized research institutes close to hotbeds of academic and biotechnology prowess is one way pharmaceutical companies are strengthening their hold on the new biology. Another way is making deals.

Merck, for one, is making deals more aggressively than it ever has before, establishing beachheads in genomics, proteomics (the science and technology of cataloguing and describing the behavior of all the proteins encoded in a particular organism's genome), and other forms of advanced bioscience. "From a pure numbers point of view," explains Ben Shapiro, "our research budget is around $3 billion a year, so we do about 1 percent of the world's biomedical research. That means, at the most simplistic level, that one hundred times as much [innovation] is going on outside of Merck as inside of Merck. Given that as a fact, what do you need to do? The answer is, we've got to look outside of Merck, voraciously, for other opportunities."

Merck has stepped up its dealmaking in the past few years; the company executed 48 agreements in 2002, compared to only 10 in 1999. Perhaps the most prominent deal has been the half-billion-dollar acquisition of Rosetta Inpharmatics. Rosetta's groundbreaking technology allows researchers to systematically analyze changes in "gene expression"—which genes are turned on or off—in the cells of both healthy and diseased tissue. The gene expression technology helps Merck researchers sharpen the focus of every step in the development of a new drug, from identifying potential toxicological problems to shaping the selection of patients for late-stage clinical trials.

A particular pattern of gene expression in cells exposed to a potential new drug molecule, for example, might give an indication that the molecule would ultimately be toxic in humans. "We realized that we didn't need to do three-month animal safety studies to start sorting the sheep from the goats here," Shapiro remarks. "We could in fact do cellular studies that would tell us quickly, by gene expressions, using Rosetta's approach, to help sort through what might be toxic later." If a gene expression pattern is associated with the progression of a disease, and researchers find that manipulating a particular drug target alters that pattern in a favorable way, it gives the researchers a strong indication that the target is a good one to aim for.

Feeling the Burn



What has the genome sequence done for me lately? If you ask Bennett M. Shapiro, the longtime executive vice president for worldwide licensing and external research at Merck, all it has done for drug companies is boost their burn rate. Shapiro explained why that is, and what drugmakers can do about it.

Much of the excitement about the Human Genome Project centered on the idea that having the genome sequence and a laundry list of new genes would help researchers develop new drugs. But so far that hasn't happened. Why not?
What you had was a lot of potential information that had to be translated into useful, functional information. All of a sudden, that number of potential targets to play with went up by several orders of magnitude. There are 30,000, 50,000 genes, maybe two or three times as many proteins as that that are functional in cells. In fact, there are so many of them that one can't just chase after everything.

How is a drug company to deal with this new glut of targets?
You really need to have good, rational approaches to deciding what you're really going to try to go for. That's always been a principle of drug discovery, but it just has been made more complex with the number of potential things to look after.

Does that make this a difficult time for drug researchers?
There's never been a better time to be a drug discoverer than today. It's just breathtaking. But the way I think it's going to play out is that one has to understand how to validate targets, how to deal with issues of safety, how to deal with issues of rapid identification of appropriate lead compounds and optimizing them into drug candidates and all that. And to do that, there's going to need to be continuing technological change.

COURTESY OF MERCK

This past February, Merck also reached an agreement with Sunesis Pharmaceuticals, based in San Francisco, to develop a series of promising compounds for the treatment of Alzheimer's disease. Using a proprietary technology called "tethering" that allows researchers to identify molecules that bind to a given drug target, Sunesis has found a number of small molecules that block the activity of an enzyme linked to one of the hallmarks of the disease—a buildup of biological gunk, known as amyloid plaques, in the brain. And Merck is getting not just the small molecules but broader rights to use the tethering technology, which it hopes will make drug discovery more efficient in other areas of research.

Shapiro says Merck is particularly interested in any technology that allows researchers to validate drug targets—that is, make clear that the targets they are aiming for play critical roles in diseases and their treatment. "If we could increase throughput here," says Shapiro, "we're going to be able to take more shots on goal and increase our probability of success."

48

deals were inked by Merck in 2002, up from 10 in 1999.

IRRATIONAL EXUBERANCE

Many people at pharmaceutical companies never bought all the hype surrounding the Human Genome Project. As Shapiro puts it, "I think it's fair to say that there was a substantial amount of 'irrational exuberance' about the genome. People who didn't know much about science felt that once you had the human gene sequence, basically you were a significant portion of the way to the goal. And anybody who really knew anything about this knew that maybe you were just beginning to start the ball game at that point. You were nowhere near the goal."

Indeed, most drug company executives appear to understand that the transformative power of genomics, proteomics, and other related technologies will take time to exert itself. Iain Cockburn, a Boston University economist who follows the drug industry, predicts that it will take on the order of a decade for the new technologies to have an impact. "The clock of drug discovery has speeded up, in part because of the culture of the biotechs," he says. "But reducing all these technologies to practice will be a long and difficult process. It's not going to shorten drug discovery to two years."

Even a slight increase in the rate of drug discovery would dramatically change the formula for success in the business, however. And that is why Novartis's new institute is merely the largest and most visible example of the rush by pharmaceutical companies to spend enormous amounts of money to gain the smallest edge from the new biology. "I'm not sure that many people know how to integrate all these aspects," said Vonderscher. But, he added, "It's the groups that integrate all these elements the fastest and the best that will be the winners." And if genomics and other new approaches can increase the industry success rate by a mere 10 percent, no one will be talking about problems in the pipeline.

Stephen S. Hall is the author of four books about biomedical technologies; the most recent is *Merchants of Immortality*.

GE FINDS ITS INNER EDISON

FORGET TAKEOVERS. ATOP THE WORLD'S LARGEST CORPORATION, JEFF IMMELT IS INVESTING IN FUNDAMENTAL RESEARCH AND MAKING IN-HOUSE TECHNOLOGY A CORNERSTONE OF GROWTH. IT'S ALL ABOUT CONTINUING THE LEGACY OF FOUNDER THOMAS EDISON.

INTERVIEW BY ROBERT BUDERI » PHOTOGRAPH BY BETH PERKINS

TECHNOLOGY REVIEW: You've upped the ante significantly on R&D, placing heavy emphasis on longer-term research and homegrown innovation. What led you to it?

JEFFREY IMMELT: We're inheriting a slow-growth economy, a slow-growth world. There's a lot of excess capacity, but companies want to grow market share and margins. And in the future, that will be done by funding innovation that reflects customer needs and developing technologies over a long period of time. I started my career selling, and I made this profound discovery that whenever I had good products to sell, I always did better than when I had lousy products to sell. So we're closing the door on a decade that was about capital markets and acquiring things and opening the door on a new period that's more about developing things. The companies that know how to develop things are ultimately going to create the most shareholder value. It's as simple as that.

JEFFREY R. IMMELT

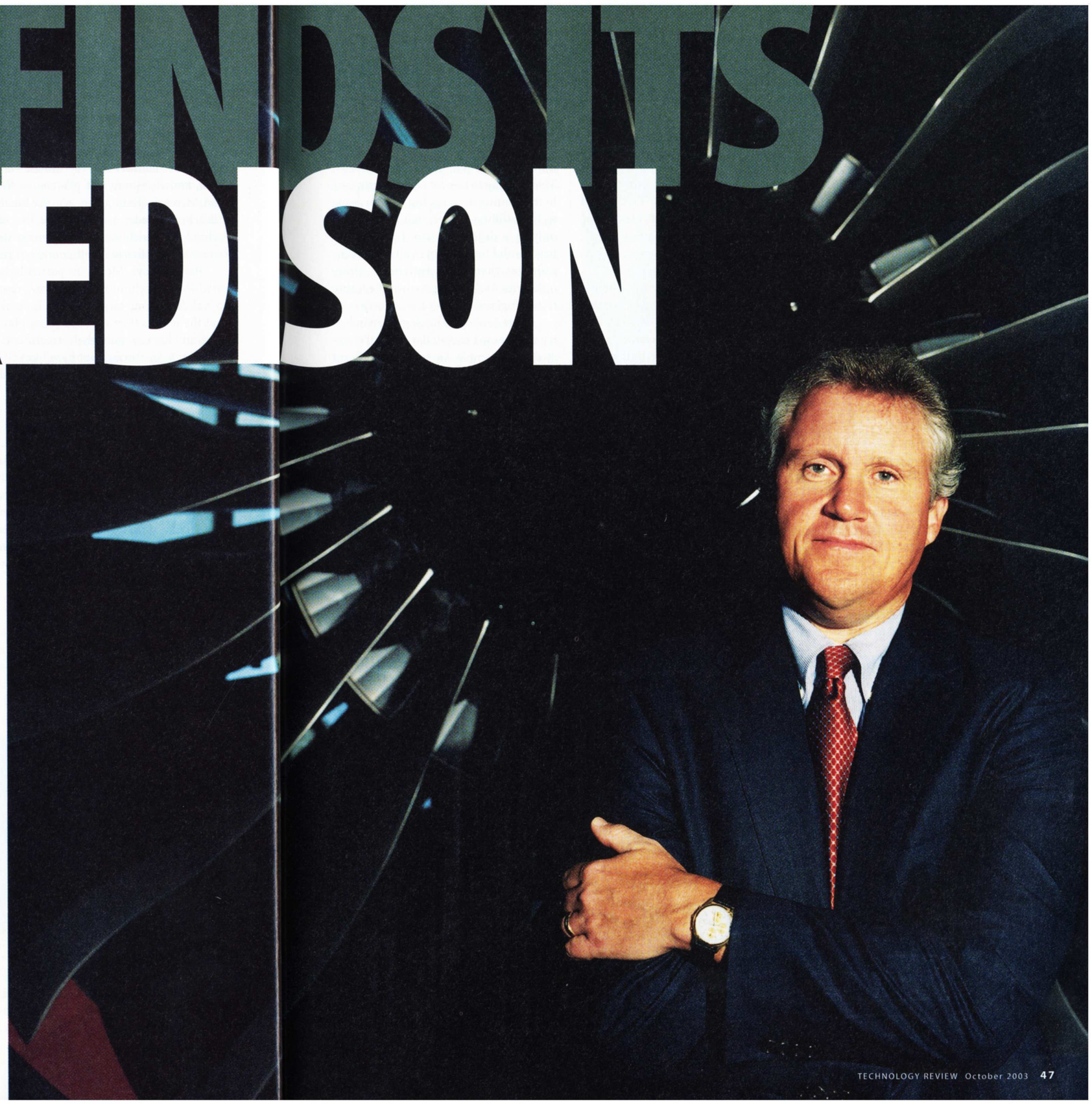
» POSITION: Chairman and CEO, General Electric

» ISSUE: Amidst tight profits and a snaillike economy, how to grow GE's highly diversified $132 billion operation, with businesses in everything from power generation to medical imaging, appliances, aircraft engines, and financial services—and preserve the company's century-old reputation for innovation.

» PERSONAL POINT OF IMPACT: Since taking over in 2000, has placed high priority on creating new businesses. Has opened a research lab in China and is building another in Germany, pushing long-term projects in molecular imaging, nanotechnology, advanced propulsion, energy, and other areas. Upped central R&D budget from $286 million in 2000 to $359 million in 2003; seeks to make GE's main lab a focal point for strategic planning.

TR: How does GE's global expansion figure in, with your new research labs opening in Munich and Shanghai?

IMMELT: The new labs bring technology development closer to our global customers and help us tap into talent that exists outside the U.S. We have three new R&D centers: Bangalore, India, which opened in 2000; Shanghai, China, which opened earlier this year; and Munich, Germany, which will open in 2004. Each place brings something different. India graduates around 10,000 electrical engineers every year, so you get this incredible wealth of talent. Our Bangalore lab is strong in computer modeling and analysis, advanced materials, and medical visualization. Then you go to Munich. The cost of an engineer



"WE'VE BEEN IN THE ENERGY BUSINESS FOR 100 YEARS. IF WE WANT TO STAY IN IT, WE'D BETTER HAVE A PRETTY GOOD UNDERSTANDING OF WHAT KIND OF TECHNOLOGIES PEOPLE COULD BE USING TO GENERATE ELECTRICITY 30 TO 40 YEARS FROM NOW."

is more or less the same as in the U.S., but the engineering schools in Germany are among the best in the world, and you get innovation in renewable energy, sensors, advanced medical imaging, and automotive technology. Plus, it brings us closer to our European customers. And then you look at Shanghai. You get a great market capability in China and a relatively economical technical base; China is doing a lot of work in power electronics, manufacturing technology, and ceramics and metallurgy. So I firmly believe in global technology development, where you can really tap into the best ideas around the world.

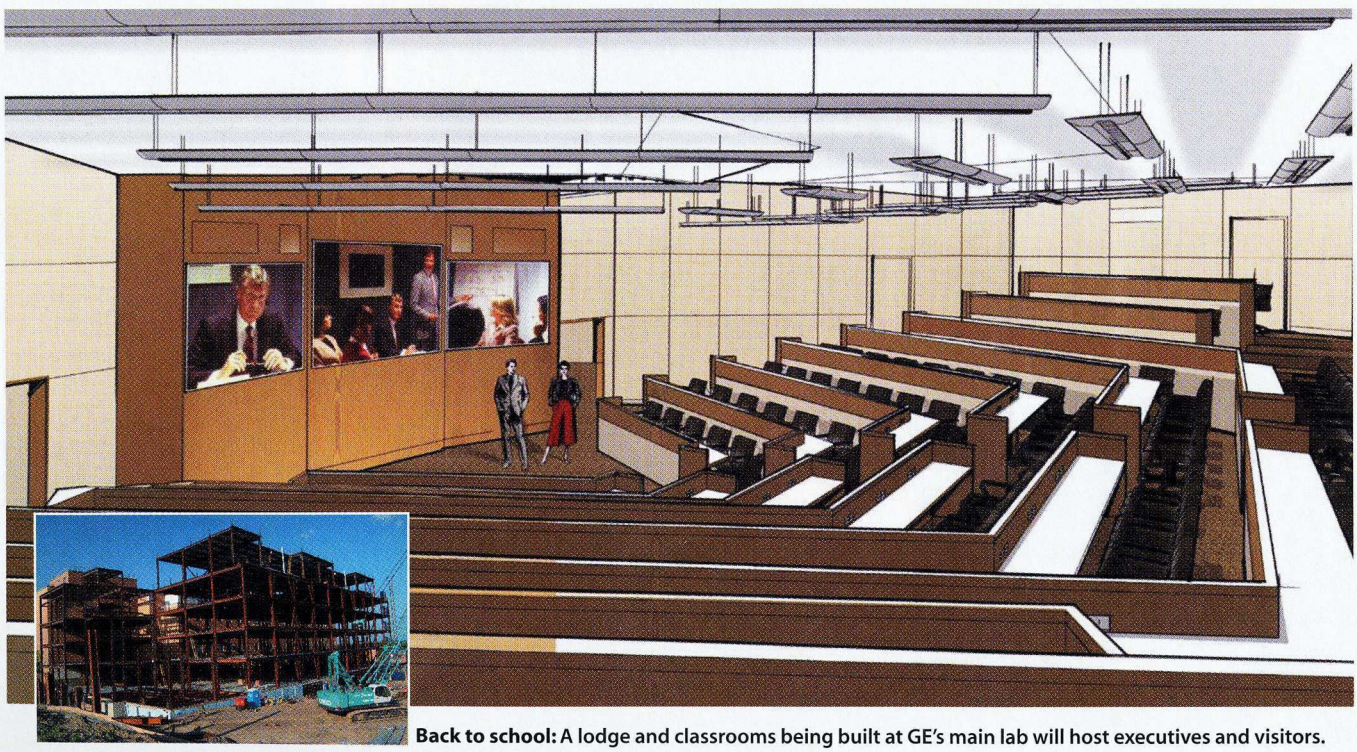
What we've insisted on is that when we globalize, we globalize products and systems and technology. So that India, for instance, becomes the world leader in a certain domain, versus just being a sliver of somebody else's program that's run from the U.S. Unless you're willing to do that, you never get the global capability you really need.

TR: You spoke of the need for GE to develop its own businesses, as opposed to acquisitions. Can you explain more fully how technology fits into your plans for growth?

IMMELT: Organic growth is the driver. I measure our teams basically on organic growth. Acquisitions is secondary to that. It's a luxury we have because we generate a lot of cash.

In GE, everybody grows up, whether they know it or not, in a technology-based company. The genius of Edison was that he was both an inventor and a very good businessman: he understood the importance of innovation that fulfilled needs in the marketplace. Let's take energy. The big market needs in energy are high fuel efficiency, competitive cost, and reducing emissions. We're looking at all the fossil fuel energies, plus wind, photovoltaics, hydrogen, nuclear, almost every possibility. Now, I sit here and say, "Will photovoltaics exist as a generator of power?" I believe the answer is yes—and GE will be a part of that. It could be in 2015, 2020, 2050, depending on innovation, the price of oil, the regulatory environment—and a lot of those things you can't predict. But we know what the needs are; it's up to us to invest in new technologies that will meet those needs. There's going to be a lot of new businesses in the coming decades, but they're going to be fulfilling a need that exists today only in a different form. I want us to have a solid foundation in all those technologies that could transform these industries. We're going to own the future technologies that meet those needs.

As we develop technologies, an industry that doesn't exist today might be created. For example, we have a significant investment in technology across the company—for our medical business, our power business, and a bunch of other businesses—around nondestructive testing and predictive failure—the ability to test and evaluate the physical structure of an asset without taking it apart. That's going to be an industry in and of itself. You're going to be able to look at a chemical plant and remotely monitor it, understand when the pipes might fail, a whole series of events that could impact your production. It's not a business we're fundamentally in today, but it's a business we will be in in five or 10 years. It's not a natural growth of any individual business, but collectively, we



Back to school: A lodge and classrooms being built at GE's main lab will host executives and visitors.

have such a great expertise in this area—that's where it grows from.

TR: This willingness to look farther out, invest over long time periods, and maybe take a few more chances, seems different from what GE has done in the past 10 or 15 years. If anything, the central lab had a reputation for shorter-term, less fundamental research.

IMMELT: Because it's so much the heritage of the company, I can't really categorize it as different. If you look at our medical business, for instance, we always have done things that have been 10 or 15 years ahead of where we needed to be. But let's say it is different: we are investing more R&D dollars on longer-range programs. I'd say one of the things that I personally believe is that I can't sit around a company like GE and see us want to go out and pay a startup $100 million for technology that if we had just spent $2 million a year for 10 years, we could have done a better job at.

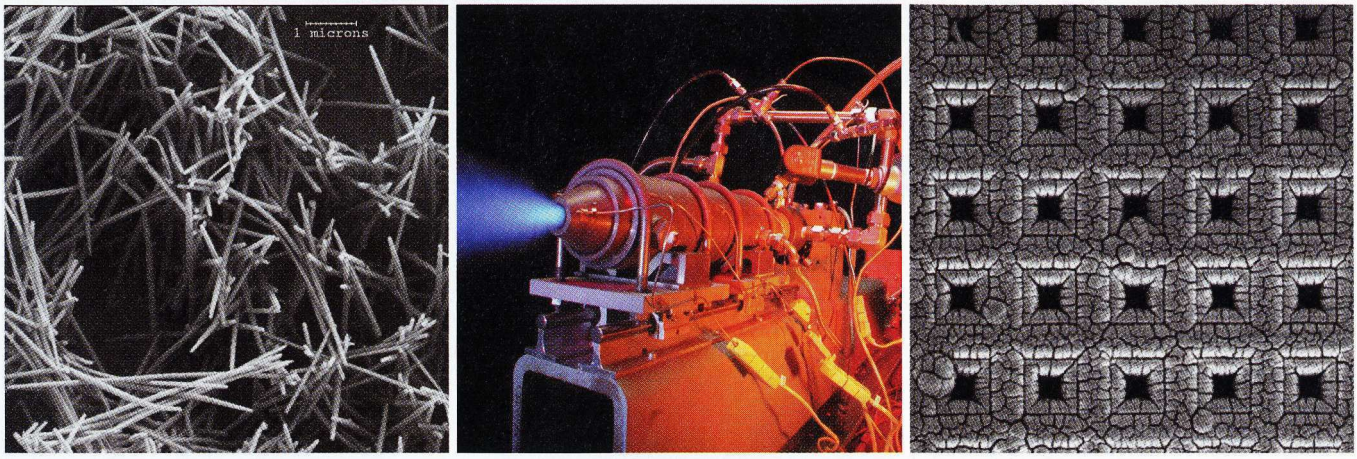
I hate that, I just hate that. I really hold our leaders accountable to figure out our markets, figure out our customers, and invest in where we see the market going. You know, I look in the mirror every day and see my banker. So I have great engineers and a good banker, and we know as much about the market as anybody else. I don't see why we can't do just as good a job of innovation as anybody else. So I do have a real hot button on that one. And I've been driving that one really hard.

TR: What areas get you most excited?

IMMELT: Molecular imaging—the ability to see disease start at the cellular level—will absolutely transform the medical-imaging business and diagnostic medicine *(see "A Sharper Picture of Health," TR September 2003)*. All the things happening in the energy industry, from wind power to hydrogen as a fuel source. And nanotechnology, because it's the materials our products are made of that make jet engines more powerful, imaging systems more accurate, and power turbines more efficient. Nano has the potential to open the door to all-new material properties that we haven't been able to achieve before.

TR: How do you pay for all this research?

IMMELT: The individual businesses con-



Basics of growth: GE's research spans (left to right) nanowires for creating new materials, advanced propulsion systems, and solid oxide fuel cells.

tract with the R&D center on enabling technology projects that let the businesses develop their next-generation products and services. That's about 60 percent of the budget. Thirty percent comes from me, for longer-range technologies—stuff five to 10 years out. The final 10 percent comes from external contracts, typically with the U.S. government.

One thing I've done is, two or three years ago our lab might be running as many as 400 projects. Now we run about 50 or 60, so we do fewer, higher-impact projects that the businesses have a clear line of sight on and interest in.

For something like nanotechnology that has the potential to impact four or five businesses but takes long-term, high-risk research to realize that potential, it's impossible for me to expect any one of our CEOs [each of GE's 13 business units has its own chief executive] to invest in it on their own. So I fund those types of programs—in nanotechnology, photovoltaics, molecular imaging, hydrogen energy, advanced propulsion. Those would be minimally $10 million a year each; some would be more than that. Typically, they would have NIH [National Institutes of Health] or Department of Energy or some kind of government funding associated with them. Inherent in it is a commitment of multiple years: these aren't things you start and stop. But by the same token, nothing is set in stone. There comes a point in time where stuff might not make as much sense, and we have to cut it, or I might have to double the bet in others.

TR: To help do all this, you announced a $100 million expansion in the global research center, near Schenectady. Can you explain the plans to also use the center to help exchange ideas between GE's businesses and customers?

IMMELT: We've always had our management development center in Croton-on-Hudson—about 50 miles [80 kilometers] north of New York City—which has been a hub of change for the company for a long time. It has been a big part of creating the culture in the company. What I've wanted to do is make our global research center also a hub for driving change. I want it to be the place where we talk about and develop our technology strategy, a place where we keep our business leaders educated about the developments in the latest technologies. So we're building facilities, like a new conference center and lodge, to enable our leadership team to spend some quality time at the R&D center. I really want a generation of leaders that are never intimidated by technology.

Our business leaders are spending time at the center learning where technology is going, while at the same time educating scientists about where the market is going and what is most important to our customers. I really want that to be part of the global research center. That way, it's not an island. One of the big fears is that you develop this blue-sky place that's totally isolated from reality. I want a whole series of leaders to be able to come through there and share that reality, while at the same time they become better technology managers. Another reason we're building the conference center and lodge is that I expect customers to be 30, 40, 50 percent of who comes up there. Customers will come there to hear about potential technologies and how they might impact their markets.

And the customers will be able to tell us firsthand how they see technologies impacting their businesses. It will help shape some of our R&D efforts and keep the voice of the customer in our technology development.

TR: Let's go back to the first question. At a time when the prevailing trend is to shorten product development cycles and hunker down, won't focusing more on longer-term technologies risk missing market opportunities today?

IMMELT: Our cycle times of developing new products shorten every year—we're in great shape on that. That is an important initiative, to fill the pipeline.

But if you look at the heart of the industrial side of GE, we are the world's preeminent infrastructure company. And much of our stuff takes place over relatively long cycles. We've been in the energy business for 100 years. So if we want to stay in it another 100 years, we'd better have a pretty good understanding of what kind of technologies people could be using to generate electricity 30 to 40 years from now. If we're going to fly people, we'd better have a pretty good understanding of that. If we're going to image people, we'd better have a pretty good understanding of that. And all that requires long-term understanding of technology leadership. It comes from the old salesman in me: it's always easier to sell the things you're selling today if you can also captivate customers with what the future brings. That's just a truism.

Robert Buderi is editor in chief of *Technology Review*.

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10 TECHNOLOGIES THAT DESERVE TO DIE

A SCIENCE FICTION WRITER'S IRREVERENT TAKE ON WHAT TODAY'S YOUNG INNOVATORS SHOULD STRIVE TO REPLACE.

BY BRUCE STERLING ILLUSTRATIONS BY TIM BOWER

TECHNOLOGIES DIE rather routinely—seen a Conestoga covered wagon lately?—but it's rare for them to be singled out and righteously put to death. Some technologies, however, are so blatantly obnoxious that the human race would rejoice if they were obliterated. A wise society would honor its young technical innovators for services rendered in annihilating obsolete technologies that are the dangerous hangovers of previous, less advanced generations. Let me offer some candidates.

1. NUCLEAR WEAPONS

ONE CAN make some sound arguments for nuclear power—medical radioisotopes are quite handy, while far-traveling spacecraft can barely function on anything less—but there is no reason for us to go on pretending that we need to fry entire chunks of continents. Not only are nuclear weapons technically clumsy, but they betray a blatant death wish better suited to al-Qaeda than a civilization.

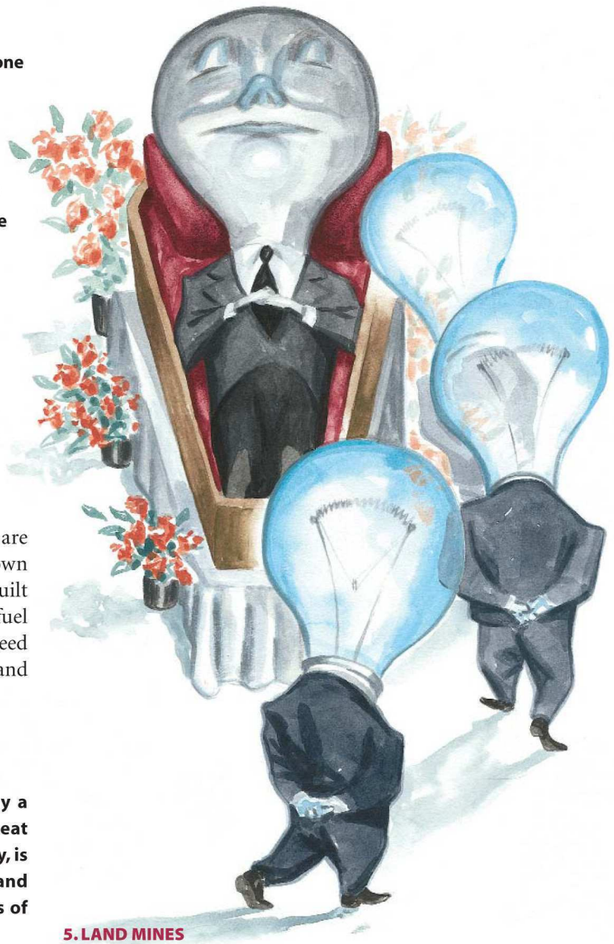
Nowadays, a well-organized state can deftly obliterate any conceivable target with exquisite GPS accuracy. Conventional "daisy cutters" and cluster bombs can be scaled up to any size or potency that the military might need. This leaves nuclear bombs with only one ideal function: terrorism. They are excellent weapons for nongovernmental predators to deploy against centers of government. They are quite useless for governments to deploy against terrorists. So why are governments still manufacturing these expensive, dangerous, easily stolen objects? If all nuclear weapons vanished tomorrow, the world's current military situation would not be affected one whit. The U.S.A. would still be military top boss. Yet we'd be much less likely to wake up one morning to find Paris or Washington missing.

2. COAL-BASED POWER

COAL ISN'T so much a "technology" as a whole school of them, all of them bad or worse. Coal was the primeval fuel of the industrial revolution. Coal powered the first steam engines, whose killer app was pumping stagnant water out of coal mines. It powered the railroads, whose killer app was moving coal.

Unfortunately, we've been doing this coal trick for some two hundred years now, and coal is getting uglier by the day. If your accountants rival Enron's, you can claim that coal is a cheap fuel. Add in acid rain, climate damage, and medical costs, and it swiftly becomes dead obvious that coal is a menace. Coal spews more weather-wrecking pollutants into the air per unit of energy than any other fossil fuel. Extracting coal destroys vast tracts of land. Coal mining is one of the world's most dangerous jobs.

If coal vanished tomorrow, we'd miss it: the U.S. would lose a quarter of its energy supplies. But that shortfall, daunting though it is, cannot compare to the ghastly prospect of blackened skies over China and seas rising out of their beds. The sooner we rid ourselves of this destructive addiction, the less we will have to regret.



3. THE INTERNAL-COMBUSTION ENGINE

I HAVE to confess that, as a former denizen of the 20th century, I'll miss the loud, soul-stirring THRAAAAGH of a two-stroke motorcycle. And liter for liter, calorie for calorie, gasoline is truly the queen of liquid fuels. Nevertheless, if you stand inside a closed garage with any internal-combustion engine, it will kill you. That is bad. Even the best such engines emit an eye-watering stink.

Internal-combustion engines are big and clumsy. They are hard to tune, and they waste a lot of effort carrying their own weight. They've got a great incumbent fueling system built into place, but they need to be replaced by hydrogen and fuel cells, technologies that are simpler, safer, and cleaner. If you need really loud, macho engine noises, why not just record them and play them on your car stereo?

4. INCANDESCENT LIGHT BULBS

IN REALITY, these sad devices are "heat bulbs." Supposedly a lighting technology, they produce nine times more raw heat than they do illumination. The light they do give, admittedly, is still prettier than the eerie glow of compact fluorescents and light-emitting diodes. But it's still a far cry from the glories of natural daylight.

Plus there's the cost of light bulbs, their fragility, the replacement overhead, the vast waste of energy, glass, and tungsten, the goofy hassle of running air conditioners to do battle with the blazing heat of all these round little glass stoves…let's face it, these gizmos deserve to vanish.

They will be replaced by a superior technology, something cheap, cool, and precisely engineered, that emits visible wavelengths genuinely suited to a consumer's human eyeball. Our descendants will stare at those vacuum-shrouded wires as if they were whale-oil lanterns.

5. LAND MINES

THE PLANET is already cluttered with well-meaning nongovernmental organizations protesting land mines. Their plaint makes perfect sense when you realize that land mines are ideally suited to blowing up peacemakers once a war is over.

During a war, few soldiers step on land mines, because mines are placed by enemies waiting with rifles. Once the armies demob, though, and armies always do, land mines don't kill combatants anymore. They kill livestock, the brighter and more exploratory kinds of children, and the men and women who wander around after soldiers, attempting to restore the planet to habitability.

SUPPOSEDLY A LIGHTING TECHNOLOGY, INCANDESCENT BULBS PRODUCE NINE TIMES MORE RAW HEAT THAN THEY DO ILLUMINATION.

ONE HATES TO SEE THIS DAZZLING TECHNOLOGY GO. BUT THERE IS LITTLE POINT IN STEPPING ONTO THE MOON, LEAVING FLAGS, AND RETREATING.

There is something to be said for the practice of automating bombs so that people can get killed without any human intervention. After all, there's a long technical trend there, and it strongly favors advanced societies with engineers over those among us who merely pick up hoes and axes in fits of tribal rage. But it's stupid to manufacture and spread lethal devices that don't know when a war is over.

6. MANNED SPACEFLIGHT

ONE HATES to see this dazzling technology go, but when one resolutely sets the romance aside, there's not a lot left. Thanks to decades of biological research, it's now quite clear that flying around the solar system is bad for one's health. Without the healthy stresses of gravity on one's skeleton, human bones decay just as they do during prolonged bed rest, while muscles atrophy. Cosmic rays blast through spacecraft walls and human bodies, while solar flares will fry astronauts as diligently as any nuclear bomb. I won't mention the fact that spacecraft are inherently rickety and dangerous, because that's a major part of their attraction.

China is about to send her first "taikonaut" into orbit, to belatedly become the world's third manned space power. As a test of national will and skill, Chinese spaceflight is vastly preferable to, say, invading Taiwan. I promise to watch Chinese manned spaceflight with great interest, and I might even buy the mission patch and decals, but frankly, there isn't much there there. There haven't been men or women out of low-earth orbit in some 30 solid years. We don't seem to miss them in any way that is quantifiable.

DVDs ARE UNBEARABLY FRAIL. ANY BENEFIT ONE GETS FROM "CLEARER PICTURES" IS QUICKLY REMOVED BY A SINGLE THUMBPRINT OR SCRATCH.

There is little point in stepping onto the moon, leaving flags and footprints, and then retreating once again. The staggering price of shipping a kilogram into orbit has not come down in decades. In the meantime, unmanned spacecraft grow smaller and more capable every year. Until we bioengineer ourselves to enjoy cosmic rays, or until we've got rockets that can lift a Winnebago made of solid lead, this technology belongs on the museum shelf.

7. PRISONS

IT'S RATHER out of style to suggest that people who transgress might be rehabilitated if treated decently. But even if criminals are to be relentlessly punished, removed from the sight of decent people, and kept in a giant, two-million-person ghetto, there are better, cheaper, and more efficient ways than the ones we have.

Newfangled electronic-parole monitors and ubiquitous computing offer plenty of opportunities. These certainly needn't be seen as sissified kinds of constraints; they could be just as cruel and unusual as anyone might like.

Lose your American internal visa (formerly known as a "driver's license") and you soon find that merchants won't take your credit, that aircraft won't transport you, that for all your sunny smiles and good behavior, you are under heavy constraints. American airports have become incarceration centers in all but name, plus you can get a drink there and listen to Muzak. So why do we go through these same ritual gestures with the iron bars, uniforms, and transport trucks? Technically, it's redundant.

8. COSMETIC IMPLANTS

THERE IS something scarily aberrant about puffing up living human flesh by implanting large amounts of an alien substance. Not that people will sacrifice vanity—of course that is out of the question—but any truly advanced medical technology would simply grow the flesh into the desired shape, using the human metabolism, as opposed to injections of window putty. Silicone's mimicry of flesh—and the same goes for gel, saline, and collagen—is too crude for genuinely cosmetic purposes.

9. LIE DETECTORS

THEY JUST plain don't work. They might have some vague use in increasing the psychological stress of a subject under interrogation, but galvanic skin response and heart rate have little to do with the process of lying. The use of lie detectors is basically a voodoo ritual that allows large institutions to lie to themselves about the trustworthiness of their employees.

Even if lie detectors did work—say, with newfangled nuclear magnetic-resonance brain scans—they would become an Orwellian intrusion. Furthermore, there would likely be a social revolution as major actors in society, from top to bottom, had to admit to fabricating their lives out of spin and wishful thinking. The official public version of our means, motives, and opportunities is severely divorced from the private world of our interior thoughts. If we were forced to confront and reveal our brain functions through technological means, most of us would soon discover that we led half-baked lives of quiet intellectual desperation, in which very little thought of any kind ever took place.

10. DVDs

THE DVD was the most eagerly adopted electronic consumer gizmo in history, but I'd feel bad if I failed to complain about the evil of these things. First and worst, DVDs are unbearably frail. Any benefit one gets from "clearer pictures"—on what HDTV superscreen, exactly?—is quickly removed by the catastrophic effects of a single thumbprint or scratch. Plus, just like CDs, DVDs as physical objects will prove to warp and delaminate.

Most loathsome of all is the fiendish spam hard-burned into DVDs, which forces one to suffer through the commercials gratefully evaded by videotape fast-forwards. The Content Scrambling System copy protection scheme doesn't work, and the payoff for pirating DVDs is massive, because unlike tapes, digital data don't degrade with reproduction. So DVDs have the downside of piracy and organized crime, without the upside of free, simple distribution. Someday they will stand starkly revealed for what they really are: collateral damage to consumers in the entertainment industry's miserable, endless war of attrition with digital media.

Bruce Sterling is a science fiction author, journalist, and cultural critic based in Austin, TX.

CULTIVATING GROWTH

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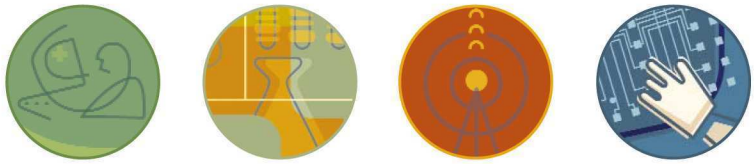

TR100

Meet the 2003 TR100, *Technology Review*'s latest selection of 100 brilliant young innovators whose vision and hard work are shaping our future.

EVER SINCE cave dwellers figured out that rocks and sticks made it easier to dig holes and gather food, technology has profoundly influenced the way humans live and work. So to catch a glimpse of technology's future—and our own—*Technology Review* looked to the people who are creating it. We combed through the rosters of universities, companies, national laboratories, and other R&D outfits around the globe to find 100 of today's most exciting young innovators: the lab dwellers, visionaries, and dealmakers whose work will utterly transform our world in the years to come. ▪ The TR100—all under 35 as of January 1, 2003—are poised at the cutting edge of computing, biotech and medicine, the Internet, and nanotech (and more). In the next 52 pages, you'll not only learn about each innovator's unique contributions, you'll also get a view of some of the major trends in each of these four key areas of technology, as seen through the eyes of the TR100. And because many of our honorees' efforts are paying off already, we've included for each technology area a table that highlights the new companies and emerging products that are the fruits of their labors. ▪ This is the third time *Technology Review* has identified 100 young innovators to celebrate, and as in the past, we've drawn on the expertise of an outstanding panel of judges in choosing our list. You'll find their names, along with those of the many writers who helped us tell the TR100's stories, on page 112. On that same page, we've provided an alphabetical listing of all 100 innovators. And starting on page 110, we revisit some of the most exciting of the 200 young people we profiled in the past, people who have already made indelible marks on technology and on our future. ▪ Yesterday, it was rocks and sticks. Tomorrow, who knows? The 100 exceptional young people you're about to meet do.

Computing

The interplay of biology and information technology is transforming how and why computing is done.

ADVANCES IN INFORMATION technology usually boil down to a few classic story lines. There's the story of Moore's Law, in which computers steadily gain performance, use less power, and fall in price. Then there is the story of how the exchange of data between far-flung computers gets easier every day. Look at this year's TR100 innovators in computing, which spans both hardware and software, and you'll see evidence of these trends at every scale, from tiny, single-electron transistors to computer grids that gird the globe. But look again and you'll also see a bold new story emerging: the increasingly productive interplay between computing and biology. ■ More and more biological processes are being understood by viewing them in terms of information processing. And computer models are increasingly helping biologists design new experiments and gain insights into the workings of complex biological systems. In turn, computer scientists are looking at living organisms as the ultimate models for new approaches in decentralized computing. All in all, it's a cross-fertilization that was practically unheard of until a few years ago.

Perhaps nowhere are advances in computing helping biology more than in the field of genomics. Consider, for example, the genome-parsing programs that **Serafim Batzoglou** has developed at Stanford University. The software takes full advantage of all the cheap computing power and memory hitting the market. "Now, we can easily hold the entire human genome in main memory," Batzoglou says. With "small clusters of cheap Pentium machines," he adds, it has become possible to rapidly search that data for specific DNA sequences. Comparable to scanning volumes of the *Encyclopedia Britannica* to locate a specific string of 10 words, this search is crucial to understanding genetic differences between individuals and between species. The biggest speedups in the search process, Batzoglou says, have come from "designing clever algorithms."

In another example of the infotech-biology convergence, startup Sana Security in San Mateo, CA, is building a computer security scheme that is rooted in the study of how organisms protect themselves from biological intruders. **Steven Hofmeyr**, Sana's founder and chief scientist, explains that studying immune systems through the lens of digital information processing has yielded several powerful algorithms that help protect banks of computer servers from hackers and computer viruses. Biology has taught researchers that software distributed across many machines that can teach itself the difference between benign activities and malicious attacks, for instance, may

BY JOHN VERITY » ILLUSTRATION BY CELIA JOHNSON


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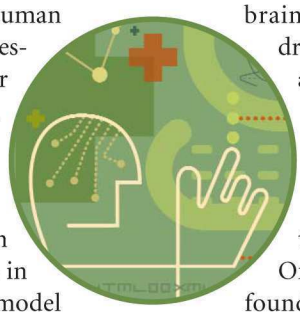
provide better security than centrally managed, hard-coded approaches. Information systems are getting too complex for humans to manage effectively, Hofmeyr says, so it's important to build software that can learn and take care of itself.

While researchers like Hofmeyr are inspired by the workings of biological systems, others are inspired by the human body itself. **Cynthia Breazeal** at MIT's Media Laboratory has built robots whose mechanical faces appear to express human emotions in response to the gestures and facial expressions of people they encounter. She's using her robot called Leonardo to explore how people and robots might one day communicate. NaturalMotion cofounder and CEO **Torsten Reil** and MIT's **Jovan Popovic** have each developed software to generate realistic animations of the human body in action, with an eye toward applications in video games and filmmaking. Reil's programs model the physics, musculature, and behavior of human bodies as they run, jump, or balance on wires. Popovic's code serves as an artist-in-a-box, instantly creating sequences of drawings as an animator drags a digital object with a computer mouse.



For some, nature is not only an inspiration but a collaborator. It has long been known, for instance, that certain molecules naturally assemble themselves into highly regular, periodic structures when deposited on flat surfaces. If researchers could figure out how to control this process, it could provide a simple way to make novel nanoscale hardware devices and materials for ultradense storage. At the University of Toronto, **Ted Sargent** has figured out how to apply electric fields to assemblies of molecules as they self-organize, prompting them to form nanostructures of a specific design. His methods could yield a way to mass-produce photonic crystals used to more precisely route light, a feat that could revolutionize optical communications.

In most areas of computing, however, it's still sheer human brainpower—not inspiration from biology—that is driving innovation. **Vipul Ved Prakash**, founder of the anti-spam company Cloudmark, has come up with a way for—potentially—millions of people to jointly decide which mass e-mails are junk. He first released his online voting mechanism, called Vipul's Razor, as open-source software that's free to use and that anyone can inspect and modify. Once the program gained a substantial following, he founded Cloudmark to produce a commercial version. "Open source gives people an outlet to publish their stuff, get lots of users quickly, and prove their product," says Prakash. "Then they have a better chance of getting [venture capitalists] to take a look and invest."

Whether the TR100 are working to bring about the convergence of biology and information technology or are worried about more mundane matters, such as spam, their work shares a goal: to expand the impact of computing. In the next few pages, you will read how they are adding to the classic story lines of information technology. TR

TR100 Startups in Hardware and Software

INNOVATOR	COMPANY FOUNDED/COFOUNDED	STRATEGY/MILESTONES
Geoffrey Barrows	Centeye (Washington, DC)	Visual sensors that use neural-like circuits to detect obstacles and guide unmanned aircraft
Ian Clarke	Cematics (Santa Monica, CA)	Software for distributed secure networking and artificial intelligence
	Uprizer (Santa Monica, CA)	Peer-to-peer software that distributes content within large organizations; raised $4 million in 2001
Andrew Heafitz	TacShot (Cambridge, MA)	Method for snapping aerial photos from small rockets and sending them wirelessly to a laptop computer
Steven Hofmeyr	Sana Security (San Mateo, CA)	Software, modeled on the immune system, that enables computers to defend against viruses and hackers; has raised $12 million from venture capitalists
Mike Horton	Crossbow Technology (San Jose, CA)	Microelectromechanical sensors, a.k.a. "smart dust," that self-assemble into wireless networks; has taken in $13 million from Intel Capital and other investments
Kevin Lee	LNL Technologies (Cambridge, MA)	Integrated photonic and optoelectronic microchips for communications and computing; has raised at least $7.1 million in seed funding
Desmond Lim	LNL Technologies (Cambridge, MA)	See above
Michael O'Connor	IntegriNautics (Menlo Park, CA)	Hands-free, Global Positioning System-based apparatus for automatically steering tractors and other heavy equipment; has raised $18 million from venture capitalists and institutional investors
Joe Pompei	Holosonics (Watertown, MA)	Narrowly focused beams of high-quality audio for use in consumer products
Vipul Ved Prakash	Cloudmark (San Francisco, CA)	Spam-filtering software for use by individuals and corporations; raised $4 million in venture funding in July 2003
Torsten Reil	NaturalMotion (Oxford, England)	Software that generates lifelike, 3-D animations of human characters for computer games and films; technology will be used in *Troy*, a forthcoming movie starring Brad Pitt
Tim Sibley	StreamSage (Washington, DC)	Software for searching and managing audio and video files that recognizes sequences of spoken words
Lorraine Wheeler	Botzam (North Billerica, MA)	Utility software for Palm-OS-based personal digital assistants

Pioneer sound.vision.soul

Ironically, a near empty entertainment center will now be the mark of a true home entertainment enthusiast.

FIND IT – With TiVo® service, you can search for, find and select individual programs. That way, you're in charge. So, no matter how busy you are, you'll never miss your favorite shows.

STORE IT – The 80-gigabyte hard drive provides you with up to 80 hours of temporary storage. So you can watch your shows whenever it's convenient. Plus, you can pause and replay live TV.

BURN IT – Programs on your hard drive can be burned onto your DVDs to create a library of your favorite shows, movies and sporting events that you can watch later on most standard DVD players.

Introducing the world's first DVD recorder with TiVo,® the Pioneer DVR-810H. Another one of our technologies that make a difference. To find a dealer near you, please visit www.pioneerburner.com.

Geoffrey Barrows, 32

Centeye

Gives unmanned reconnaissance planes insect vision

IF YOU followed the recent wars in Afghanistan and Iraq, you've likely heard of unmanned aerial vehicles such as the U.S. Army's Predator. These craft allow hostile-area reconnaissance with no risk to pilots, who use Global Positioning System-based navigation to guide them remotely. Precision guidance, though, can be difficult from afar. Enter Geoffrey Barrows, founder and president of Centeye, a three-year-old Washington, DC, company that develops "bio-inspired" microelectronics. Centeye is commercializing optic-flow sensors, chips designed to help unmanned aerial vehicles navigate autonomously by endowing them with the kind of depth perception exhibited by flying insects. The chips, which Barrows developed between 1997 and 2000 while working for the U.S. Naval Research Laboratory, compare objects' rates of movement through the visual field to deduce their relative distance. With contracts from the U.S. Defense Advanced Research Projects Agency and the Naval Research Lab, Barrows is working to reduce the sensors' weight to just a few grams; he aims to deploy them in small, fast-moving robot planes within three years.

Serafim Batzoglou, 30

Stanford University

Devises powerful tools for assembling and analyzing genomes

SCIENCE HAS fascinated Serafim Batzoglou since he was 12, when he watched Carl Sagan on TV, at home in Athens, Greece. Today, Batzoglou is unlocking the mysteries of the genetic structure of organisms, and he has recently led development of two important programs for deciphering genomes. Arachne, released in 2002, was the first widely available tool for assembling full genomes from fragments of genes. Researchers used it to assemble the mouse genome, creating a blueprint for studying the human genome (mice and humans share 95 percent of their genes). Scientists also used Arachne to sequence another scientific workhorse, the fruit fly. The second program, Rosetta, helps compare the human and mouse genomes. Although Batzoglou's algorithms draw great praise, he says he's simply lucky his programming skills can be applied to biology. Now a Stanford University assistant professor of computer science, Batzoglou heads development of Lagan, a software tool for aligning long sequences of DNA so scientists can compare the genetic structures of humans and other creatures. Batzoglou is not a biologist, but his work may help rewrite the book on evolution.

Ian Clarke, 26

Cematics

Pioneered software that delivers Web files quickly, anonymously

IAN CLARKE didn't set out to ignite a debate about Internet free speech and copyrights. But that's what happened in 2000 when he released Freenet, a free program that shuffles files among Internet-connected computers, enabling people to store and retrieve data easily and anonymously. Maybe it was the fact that, unlike Napster and other peer-to-peer file-sharing systems that rely on observable central indexes, Freenet makes it almost impossible for censors or copyright owners to trace files. Maybe it was the uncompromising philosophy the County Meath, Ireland, native readily shared: "You cannot have freedom of communication and enforce copyright law." Yet Clarke says he designed Freenet mainly to test a technical idea he hatched as a University of Edinburgh undergraduate: that a network capable of replicating documents and storing them in multiple locations would bring files closer to frequent users, speeding their delivery. Enthusiasts have since downloaded close to two million copies of Freenet. In 2001 Clarke raised $4 million to start Uprizer in Santa Monica, CA, which sells corporate information management software based on Freenet. He's now cofounder and CEO of Cematics, also in Santa Monica, a peer-to-peer product development and consultancy company.

Cynthia Breazeal, 34

MIT

Constructs robots whose expressive faces convey humanlike emotions

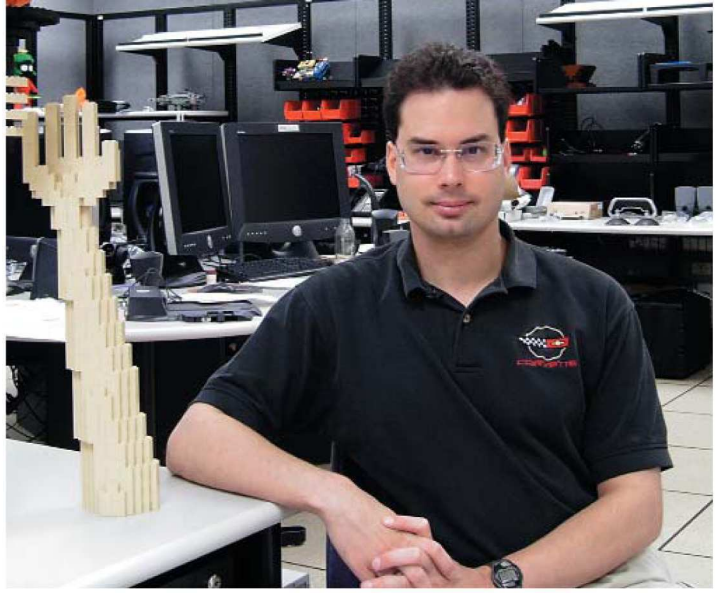
PEOPLE OFTEN ask Cynthia Breazeal, director of the MIT Media Laboratory's robotic-life group, whether robots will take over the world. "I'm like, 'Oh, go see a movie,'" she laughs. Nonetheless, there's something Hollywood about Breazeal's work. She builds expressive robots that exhibit socially appropriate emotional responses, attracting media attention as well as advancing artificial-intelligence research. For her doctoral thesis, Breazeal constructed Kismet, a bright-eyed mechanical head that reacts to human voices, movements, and expressions with smiles, frowns, and raised eyebrows. Her latest robot, Leonardo, a collaboration with the Stan Winston Studio, of movie special-effects fame, is a 75-centimeter-tall creature. The furry bot's 60 small motors produce fluid movements and subtle facial expressions; it also has pressure-sensitive "skin," microphones, a speech synthesizer, and camera "eyes" that track people's faces and gestures. Unlike other robots, whose actions are driven by programmed routines, Leonardo learns tasks by assessing humans' expressions and imitating their movements. Breazeal calls it "the most expressive robot today," and because she believes "socially intelligent" robots could become actors, or helpers for the elderly, she is conducting studies of human-robot interaction. Her lab is also helping NASA build a "robonaut" space assistant that might one day perform maintenance tasks in space.

FURNALD/GRAY (BREAZEAL); COLLABNET (BATZOGLOU); PETER MENDENHALL (DEHON)

André DeHon, 35

Caltech

Designs architectures needed to build practical molecular computers



CALTECH COMPUTER science professor André DeHon is changing the architecture of integrated circuits—and it needs changing. Conventional circuit elements are nearly as small as they can be, so materials scientists are fabricating nanowires 10 times smaller to replace them. DeHon described how to chemically modify the ends of nanowires so that the much larger wires used in conventional circuitry could address them individually. He then showed how to arrange such wires into working circuits, even within the limitations of existing lab techniques, and he has developed an architecture for building a general-purpose computer from them. Moreover, his processor can be reprogrammed to perform different computing tasks that would ordinarily require distinct architectures. This extends the work DeHon did as an MIT graduate student on reprogrammable semiconductor chips, a technology commercialized by several undergraduates he supervised, whose company, Silicon Spice, was acquired by Broadcom for $1.2 billion. "André's work is striking," says Harvard University nanotech pioneer Charles Lieber. "After reading it one must say, 'Yes, this idea of molecular computing is indeed a real possibility, not just hype.'"

Kathryn Guarini, 31

IBM

Fabricates three-dimensional integrated circuits that could vastly increase computer power

"REMARKABLE" IS how Stanford University professor Cal Quate describes his one-time PhD student Kathryn Guarini. In the mid-1990s, Guarini and Quate developed a lithography technique that let engineers pattern integrated-circuit features smaller than 100 nanometers, which packed more circuits, and thus more power, onto chips. Since 1999, when she joined IBM Research, Guarini has led Big Blue's development of three-dimensional circuits—a semiconductor frontier. For decades, designers have made transistors smaller but have continued to place them side by side in a single layer. Guarini's techniques can stack transistors in two or three layers, vastly increasing the number that fit on a chip. She has also shortened the metallic connections between transistors, accelerating processing speeds. Challenges remain, including how to limit the heat a 3-D chip produces. But colleagues predict Guarini will prevail. Says fellow IBM researcher Philip Wong, "Whatever she touches she turns into gold."

Daniel Gottesman, 33

Perimeter Institute

Works to improve quantum computers so they can speed drug design and perform other massive computing tasks

DANIEL GOTTESMAN is increasing the chances of building quantum computers that could solve certain large-scale computing problems much faster than current-day machines. Atomic particles can exist in many states at once, and if those states can be controlled, they could provide far more computational power than the simple on-off states of electronic bits. The problem is that quantum computer elements are highly susceptible to errors. While a grad student at Caltech, Gottesman helped develop a systematic method for correcting those errors, thereby stabilizing quantum computers. His methods are used worldwide by researchers designing the first rudimentary quantum machines. Now a research scientist at the Perimeter Institute, a nonprofit research facility in Waterloo, Ontario, Gottesman is writing protocols that will use quantum mechanics to provide extremely secure data encryption—in part because quantum computers will be powerful enough to break current encryption codes. Although practical quantum computers are still years away, Gottesman says their computational speed could "revolutionize" the design of drugs and new materials such as high-temperature superconductors.

Vic Gundotra, 34

Microsoft

Sparked Microsoft's change to .Net

IN 1991, Vic Gundotra, a 21-year-old programmer at Microsoft's Washington, DC, office, showed some of his demos to Steve Ballmer, then Microsoft's head of sales (and now CEO). Soon after, Gundotra was moved to Microsoft headquarters in Redmond, WA. There, Gundotra and colleagues ran the skunk works project that resulted in a new architecture for supporting company software applications across many kinds of computers; now known as .Net, it won out over several established projects. In 1999, Gundotra also wrote the code for the network software that underlies .Net—which crystallized "Web services" for Ballmer and Bill Gates. The code sparked Microsoft's decision to reorient all its software toward the Internet. Indeed, Microsoft's next PC operating system, Longhorn (due in 2005) will be driven by .Net. Gundotra is a born proselytizer for technology: he uses a tablet PC to take notes during church. He doesn't know if he'll stay at Microsoft forever, but he says, "If you want to change the world, it's much easier to do it at Microsoft."

Andrew Heafitz, 34

TacShot

Invented inexpensive rocket-based surveillance systems

ANDREW HEAFITZ acquired his first patent—for a high-speed shutter on a balsa wood camera—at age 19. Since then he has designed electric vehicles, invented a low-cost rocket engine, and developed a plant growth experiment that flew on two space shuttle missions. His MIT undergraduate thesis centered on a remote-control aerial-photography system he built using a Nikon camera and a helium balloon. While he was a mechanical engineering master's student at MIT, he installed a tiny, off-the-shelf video camera inside the nose of a small rocket he'd designed. He called the device TacShot and in 2001 launched a company of the same name in Cambridge, MA. The 350-gram self-propelled rocket travels to heights of 100 meters, radioing images of the earth to a ground-based laptop. Heafitz's software assembles the pictures into a 360-degree mosaic of the launch site. TacShot could be carried in a soldier's backpack and deployed for aerial reconnaissance or used to assess damage at disaster sites. Heafitz won the 2002 Lemelson-MIT Student Prize and invested part of the $30,000 award in his company. With a U.S. Air Force contract to conduct proof-of-concept demonstrations, Heafitz has TacShot—and his career—on a successful trajectory.

Ayanna Howard, 31

NASA Jet Propulsion Laboratory

Writes programs that more intelligently guide the actions of robots

ELECTRICAL ENGINEER Ayanna Howard sees a future in which humans and machines work together to explore new terrain. Today's planetary rovers—suitcase-size robots that move on wheels—must be remotely controlled by human operators, a labor-intensive and imprecise process. So Howard, who works at NASA's Jet Propulsion Laboratory in Pasadena, CA, developed artificial-intelligence software that mimics the decisions humans make about where to land spacecraft and how to navigate robots safely. Loaded onto a rover's computer, Howard's software can process information from maps and video cameras and automatically find a safe path between two points, in real time. The rover can thus avoid craters instead of trying to negotiate their edges—at great risk to multimillion-dollar equipment. Rovers equipped with Howard's software are now used by forest rangers in Idaho to map logging areas. They could also assist rescue operations that explore buildings shattered by earthquakes or bombs. In 2001, Howard won the Lew Allen Award, JPL's highest honor for leadership and innovation.

Steven Hofmeyr, 35

Sana Security

Devised software that roots out security threats to a network's operating system

WHEN INVESTORS backed Sana Security in San Mateo, CA, they took out $1 million in insurance on chief scientist Steven Hofmeyr, because his ideas about computer network security were their most valuable asset. Sana Security ("sana" is Esperanto for healthy) treats intranets and local-area networks much the way the human immune system treats the body: when abnormal activity occurs, Sana software recognizes the problem, isolates and analyzes it, then attempts to fight it off. Network security typically relies on human administrators who often arrive too late to stop intrusions (in January the Slammer virus reportedly infected 75,000 machines within 10 minutes). Other tools, such as software updates, arrive after the fact and can be expensive. Sana's Primary Response product resides on each computer within a network and continuously interrogates vulnerable applications, such as e-mail programs, at the operating-system level. When it detects abnormal behavior—hackers looking for loopholes, say—it stops the activity, then notifies a system administrator. Within two months of the program's release, several large organizations became customers, including NASA .

Mike Horton, 29

Crossbow Technology

Engineers tiny sensors that can be spread like crumbs around a battlefield or factory

MIKE HORTON is yanking the wires out of your life. His company, Crossbow Technology in San Jose, CA, makes truckloads of solid-state wireless sensors no larger than pagers. Within a year, he promises, they will be as small as bottle caps. In some cars, Crossbow's sensors already report acceleration and engine pressure data to engine controllers. In aircraft, they are replacing the larger, less reliable, airframe-mounted mechanical gyros that correct for altitude, roll, and drift. But Horton, who holds two patents, plans to storm the wireless field with "smart dust": sensors the size of rice grains. Sprinkled around a battleground or office building, the sensors would network themselves and analyze the environment, checking for vibrations that could indicate the passing of an enemy convoy, or airborne chemicals from an industrial spill. Having raised $13 million from Intel and other investors, Horton has partnered with mentors at the University of California, Berkeley, to write software for the motes, even as he works on reducing their size and cost. Horton believes billions of unnoticed dust sensors could transform society: "It's a quiet revolution," he says.

DONNA COVENEY/MIT (HEAFITZ)

Kevin Lee, 31

LNL Technologies

Integrates photonics and electronics on chips to speed telecommunications

AS A 16-year-old South Korean émigré living in a gang-ridden Los Angeles area, Kevin Lee had to face the threat of daily violence. That situation, he says, "gave me drive." In 2001, that drive prompted him and fellow TR100 honoree Desmond Lim *(this page)* to start LNL Technologies in Cambridge, MA, to revolutionize telecommunications. Frustrated by slowdowns that occur when fiber-optic signals are converted to the electrical signals that go into homes and offices, researchers had long tried to fashion circuitry that would manipulate light and speed up telephone, data, and video services. During his PhD studies at MIT, Lee crafted tiny optical routers and connectors that fit on a single chip. Building on that work, LNL has made prototype chips that integrate up to 10,000 photonic and optoelectronic functions within one square centimeter. The optical chip can be mass-produced and, the founders maintain, is far more powerful than other companies' prototypes. "Optics is the industry of the future," says Lee, vice president of engineering. "I want to be part of making that happen."

Desmond Lim, 32

LNL Technologies

Develops high-volume manufacturing lines for making optical chips into commodities

SINGAPORE-BORN Desmond Lim likes to convert scientific advances into marketable products. As cofounder of Cambridge, MA-based LNL Technologies with fellow TR100 member Kevin Lee *(this page)*, Lim aims to transform the company's groundbreaking optical-chip prototypes into inexpensive commodities that will upgrade data transmission over phone lines and the Internet. To that end, chief technology officer Lim has designed a fast-turnaround process for prototyping optical components such as waveguides, filters, and multiplexers, and he has developed practical, high-volume manufacturing lines to make chips for the telecommunications industry. When LNL demonstrated its flagship chip in December 2002, the *Wall Street Journal* said it "could one day become the Pentium processor of light signals." The company is now setting up field tests and talking to manufacturers about building LNL's chips. "We are leveraging what is known about standard silicon chips and putting our ideas on top," Lim says. "We are past the inspiration phase and are now in the sweat phase: moving toward mass production."

Michael O'Connor, 33

IntegriNautics

Designed an automated tractor steering system that is saving farmers bushels of money

AS MICHAEL O'Connor was completing his Stanford University PhD in aeronautics and astronautics, he realized that the Global Positioning System so central to his studies could save farmers millions. O'Connor designed a system that could guide a tractor, combine, or harvester to within three centimeters of a specified path. Upon graduating, he cofounded IntegriNautics in Menlo Park, CA, to commercialize it. The system consists of a small box installed in a tractor cab to control its steering mechanism, plus a touch screen, antenna, and GPS instrumentation. Once the farmer programs the path on the screen, the setup allows for hands-free operation that is more accurate than manual steering—and more economical, since even slight deviations can cost thousands of dollars in wasted fuel, fertilizer, and pesticides over many hectares. Although the farmer has to sit in the cab to watch for unpredictable obstacles, like animals, he can do other work while there. The system also allows operation during fog or at night. O'Connor has sold more than 400 of the $45,000 AutoFarm units. "Half the new tractors in the U.S. will have this technology within ten years," says Stanford professor Brad Parkinson, a GPS pioneer who supervised O'Connor's thesis.

Joe Pompei, 30

Holosonics

Delivers "spotlights" of sound for use in concerts, museums, and automobiles

JOE POMPEI founded Watertown, MA-based Holosonics on what many acoustics experts called a crackpot idea: directing sound in a narrow beam. But Pompei says his attitude was, "this is too cool not to work." He developed the initial technology in 1999 at MIT, the only school that gave him the green light on his PhD proposal. Within three months, he had a prototype of Audio Spotlight. The system includes a processor and a pizza-pan-sized transducer. First, the processor compresses the long wavelengths of an audible frequency into millimeter-long wavelengths of inaudible ultrasound. Then the transducer transmits the now tightly focused signal. In the air, the ultrasonic waves begin to elongate and regress to the original audible frequency, but only within the confines of a narrow beam. At distances of up to 200 meters, listeners in the beam's path hear sound clearly, but those mere meters away from them do not. Dozens of groups have adopted the system: rock band U2 is experimenting with it to direct music at concerts; it's used in museums and trade shows; and DaimlerChrysler installed it in Maxxcab truck models to provide personalized audio zones for passengers.

THE *STRAITS TIMES* (LIM)

Jovan Popovic, 30

MIT

Makes simpler, more powerful animation tools for novices and professionals

AS AN undergraduate, Jovan Popovic found that animated illustrations of math-problem solutions helped him master complex concepts. But animation is tedious and expensive. So Popovic, who grew up in Yugoslavia and is now an MIT assistant professor, set out to make it easy and affordable for neophytes and professionals alike. He developed software that works like the drag-and-drop feature in word-processing programs. To show, say, a hat flipping through the air and landing on a coat rack, the creator simply moves the hat with a computer mouse, and Popovic's program generates the appropriate animated movement. "He has made significant progress toward solving one of the key problems in animation: to make it look natural and control it at the same time," says Andrew Witkin of Pixar Animation Studios. The entertainment industry should benefit, but Popovic wants to reach teachers, children, and educational filmmakers. He isn't sure whether to license his software or start a company to develop it. Up next: programs that create animation in response to verbal commands.

Thomas Reardon, 34

Openwave

Tailors Internet applications to cell phones

MICROSOFT'S ORIGINAL Internet Explorer development team consisted of one person: Thomas Reardon—or just "Reardon," as he's generally known. As Internet mania grew, so did Reardon, from programmer to program manager, sifting through hordes of unproven technologies and emerging standards, deciding which to adopt or reject. His work culminated in Explorer 3.0, the first Microsoft browser sophisticated enough to compete with Netscape Navigator. Reardon spent the next four years working with standards bodies, driving Microsoft's move away from proprietary technologies and toward the open standards that enable software interoperability on the Internet. Today Reardon is a general manager at cell-phone software supplier Openwave in Redwood City, CA, where he's waded into the middle of the next browser war. "We're trying to kill this mentality that smart phones are just PCs ported to cell phones," he says. Instead, he is directing Openwave toward software tailored to just the applications customers seem to want—such as picture messaging and the short-message service. That strategy has paid off: more than 80 percent of U.S. cell phones now use Openwave's wireless-Web browser, and the company expects sales this year to top 180 million units.

Torsten Reil, 29

NaturalMotion

Employs simulations of human movement to create realistically animated characters

IT MIGHT be surprising to find a biologist pushing the frontiers of computer animation. But Torsten Reil is bringing cheaper, lifelike digital characters to video games and films. As a doctoral researcher in neural systems at the University of Oxford, Reil programmed computer simulations that mimicked human and animal movement, and in 2001 he cofounded NaturalMotion in Oxford, England, to commercialize that work. To create characters that move realistically, conventional animators draw extensive series of frames that are played back—repetitively—in set sequences. But Reil wrote software that an animator uses to program a nervous system for a character he or she draws just once. The code makes the character's body obey the laws of physics and react automatically to changing on-screen situations. NaturalMotion's first product is already saving game developers and visual-effects companies thousands of dollars by accelerating animation, Reil says. Look for his characters in the upcoming Hollywood epic *Troy*. Reil recently won a grant from the British government to model the gaits of children with cerebral palsy, to help doctors determine the neurological basis of the disorder.

Vipul Ved Prakash, 25

Cloudmark

Developed free and commercial software filters that fight spam

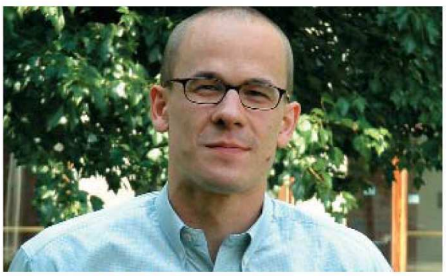
IN 1997, Vipul Ved Prakash dropped out of Delhi University "for want of undisturbed coding time," as he puts it. He then cofounded Sense/Net, one of India's first privately owned Internet service providers, but soon encountered the scourge of spam. Customers paying by the minute for their connections complained they were wasting time deleting unwanted e-mail. So Prakash developed Vipul's Razor, a spam-fighting, open-source software tool available online for free. Thousands of users downloaded the "collaborative filter" program, which allowed them to keep messages or move them into spam folders. Vipul's Razor transmitted those decisions to a central server, and if a majority of users discarded a given message, it would thereafter be blocked for the entire group. After moving from New Delhi to California in 2000, Prakash worked for a time at Napster and then cofounded Cloudmark with Jordan Ritter, Napster's former software chief. The San Francisco startup adapted Vipul's Razor into a tool called SpamNet that today boasts 500,000 users. Initially free, it now costs $3.99 per month. "When a new person joins," Prakash says, "they get the benefit of the entire community." Cloudmark also markets Authority, a corporate version of SpamNet.

Maximilian Riesenhuber, 33

MIT

Programs computers to recognize objects the way the human brain does

THE HUMAN brain can recognize a dog as a dog, but teaching a computer that trick is daunting. As an MIT postdoc, Max Riesenhuber researched the brain's object recognition processes, then led a team that wrote software to mimic them. Called HMAX, the program is accurate enough to save physiologists time and money in studying brain disorders. To test the model, researchers might show it an illustration of a composite creature, such as a catlike dog. HMAX categorizes the animal's features as more or less catlike or doglike, sums those probabilities, and issues judgments remarkably consistent with human subjects'. Now, scientists are using HMAX to craft better experiments to help explain brain disorders like prosopagnosia—the inability to recognize faces. Unraveling such afflictions is Riesenhuber's main goal. But his software also advances computers' ability to recognize objects, a key to artificial intelligence. HMAX might even help recognize satellite images. Riesenhuber, founder of MIT's Motorcycle Club, is also a principal of GeoPhoenix in Cambridge, MA, which markets a handheld computer interface that can access content by zooming and panning, helping users navigate small screens.



Heike Riel, 32

IBM

Built large, bright, organic video displays using materials dismissed by contemporaries

HEIKE RIEL left a furniture-making apprenticeship to study physics. A PhD later, she has built the world's largest full-color display that uses organic light-emitting diodes (OLEDs)—paving the way for a new generation of vivid-color, affordable, flat-panel televisions and computer monitors. Her 20-inch screen is brighter and more energy efficient than any other screen on the market. Cell-phone displays and other small screens have used OLEDs for streaming video, but larger-scale applications have proven elusive. In a large screen, each of millions of light-emitting pixels requires several transistors, and the transistor matrix had been difficult to manufacture uniformly. Researchers had steadfastly tried to improve the polycrystalline-silicon transistors, claiming that the alternative—amorphous silicon—would break down at the high currents needed for pixel emission. But Riel and her colleagues fashioned the OLEDs at IBM's Zürich lab so that inexpensive amorphous-silicon transistors drew less current and, therefore, remained stable and generated far less heat. Riel, in particular, tinkered with the width of the pixels' thin organic layers, allowing significantly more light to be emitted. "People didn't believe it could be done," she says.

Linda Rottenberg, 35

Endeavor Global

Helps entrepreneurs in emerging nations turn innovations into businesses

LINDA ROTTENBERG believes that startups are the best way to create jobs and stimulate growth in economically struggling nations. To prove that contention, she cofounded Endeavor, a nonprofit that helps entrepreneurs in emerging countries access networks, training, and everything else they need to convert innovative ideas into companies. Endeavor invests no money itself. Instead, CEO Rottenberg and five other New York-based staffers coordinate 24 employees in Argentina, Brazil, Chile, Uruguay, and Mexico—and soon in South Africa. Those employees encourage prominent local businesspeople to find funding, give advice, and otherwise open doors for entrepreneurs. In the past year Rottenberg's group has developed Web chat rooms where executives and entrepreneurs can compare notes. Endeavor claims that since 1997 it has supported 121 companies, which have generated more than 9,000 jobs and $363 million in revenue. Startups that are profitable within a few years often reward Endeavor with a small percentage of revenues or equity. Endeavor's notable technology startups include Patagon.com, an Argentine online finance pioneer that was sold for $700 million, and Taho, a Brazilian wireless-communications company. "People worldwide with good ideas are calling us every day," Rottenberg says.

Ted Sargent, 30

University of Toronto

Fashions photonic circuits that could speed voice and data to homes

TELECOM NETWORKS are half-hare, half-tortoise. Conversations and data blaze down fiber-optic cables but slow to a crawl when they encounter electronic switches at network junctions. Photonic crystals, which can manipulate photons much as semiconductors manipulate electrons, are the best hope for clearing such roadblocks. While others are exploring them, Ted Sargent is close to building practical devices. Sargent came to the University of Toronto as a grad student in 1995, joined its faculty in 1998, and in three years was awarded a coveted Canada Research Chair position. His chief advance is a process to specify and guide the growth of photonic crystals—a mix of electrochemistry, microchip fabrication, and holographic printing. Sargent etches a holographic pattern into an electrically conductive film that coats a glass plate. Then he electrifies the film, generating a holographic "tractor beam" that attracts latex beads and stacks them into a photonic crystal. Sargent has fashioned hair-thin rows of crystals that could act as circuits, and Nortel eagerly awaits proof they can manipulate photons. If so, photonic crystals could speed up the telecom network, including the "last mile" of cable to homes.

Tim Sibley, 27

StreamSage

Serves up customized audio and video gems

A YEAR after leaving Swarthmore College, where he helped fellow undergraduates engage in scientific communication by cofounding the *Journal of Young Investigators*, Tim Sibley had an insight about a related form of communication: conferences. "What scientists are truly interested in," he explains, "could be just 20 minutes of one lecture out of a hundred hours at a conference." A simple way to find relevant morsels within audio or video conference recordings would be a boon. So the mathematics and physics major secured $2 million from the National Institute of Standards and Technology to start StreamSage in Washington, DC. Sibley uses computational-linguistics techniques to automatically create a searchable index of an audio or video recording and find material relevant to any given topic. Today NASA and Harvard Medical School use his programs to provide access to streaming-video archives. Other customers might include media companies, which seek better ways to manage digital video. Next, Sibley plans to enlist speech-processing technology to stitch together personalized audio newscasts from the Web's welter of news. "More than just an audio Google," Sibley says, this system will put items in context.

Alex Vasilescu, 32

New York University

Transforms computers' ability to recognize human faces

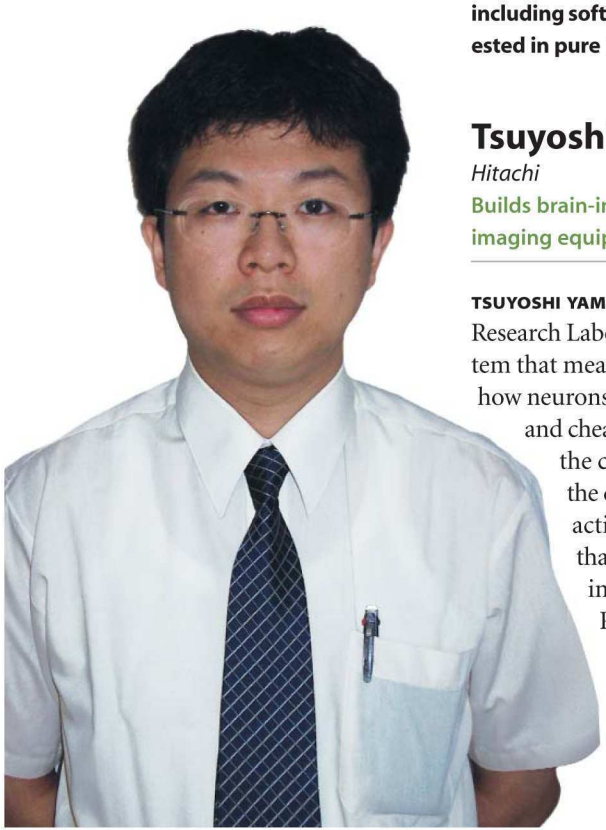
THE TROUBLE with facial-recognition software is faces. A computer probably wouldn't recognize Osama bin Laden if the lighting or his expression didn't match those in a database image of him. Using a specialized form of mathematics called tensor algebra, Alex Vasilescu—a research scientist at New York University and a computer science PhD candidate at the University of Toronto—has developed breakthrough recognition algorithms called TensorFaces. The algorithms promise to enhance computers' ability to match multiple characteristics of a face in ways that overcome vagaries of shading, angle, or expression. The U.S. Department of Defense is funding Vasilescu's research because of its antiterrorism potential. She can also generate "motion signatures" on the basis of a person's gait—walking, dancing, or running. Such gait changes can indicate the onset of certain illnesses. Finally, Vasilescu's algorithms could help computers impart realistic textures to images of hair and fabric, which could yield better graphics for video games and movies.

Lorraine Wheeler, 33

Botzam

Codes software that makes handheld computers handier

LORRAINE WHEELER is forever moving on to the next big thing. As a 22-year-old software engineer at GE Medical Systems, she devised a process to improve the signal-to-noise ratio of magnetic-resonance imaging. Her patented innovation helped clarify results for doctors who rely on such images to diagnose disease. Then, with a mere $5,000, the 27-year-old Wheeler founded Actual Software above a pizza shop in Andover, MA, and created MultiMail, one of the first e-mail programs for Palm handhelds. With MultiMail, business travelers could use their personal digital assistants to send and receive e-mail on the road. Upon its release in 1998, MultiMail's free version was downloaded 1,000 times per hour, and the full-featured version was so successful that Palm eventually bought Actual Software for $4 million. In 2002 Wheeler founded Botzam. The startup, housed in more comfortable commercial digs in North Billerica, MA, is developing new applications, including software that lets users back up their handheld data on removable storage cards. "I'm interested in pure innovation," Wheeler says. "I follow the market wherever it moves."



Tsuyoshi Yamamoto, 33

Hitachi

Builds brain-imaging machines that are faster and cheaper than magnetic-resonance imaging equipment

TSUYOSHI YAMAMOTO is steering his way through the brain. Since joining Hitachi's Advanced Research Laboratory in Hatoyama, Japan, in 1997, he has codeveloped an optical-topography system that measures changes of concentrations of hemoglobin in the brain, providing insight into how neurons process language, images, and movement. Yamamoto's device, which is easier to use and cheaper than magnetic-resonance imaging (MRI), beams light through the skull and into the cortex, the brain's outer layer. By charting the intensity of the light reflected back by the cortex, the machine gauges changes in blood cell concentrations—indications of brain activity. The instrument, which looks like a beauty salon dryer, is less motion sensitive than MRI equipment, so rather than lying flat, patients are seated for scans. Now on sale in Japan, the system has received U.S. Food and Drug Administration approval. Patients robbed of muscle control by neurodegenerative disease can communicate via Yamamoto's gear, which can sense the brain's "yes" and "no" responses to questions. He hopes his device will further understanding of language processes. "We don't know so much about the brain," he says. "I would like to find new functional areas."

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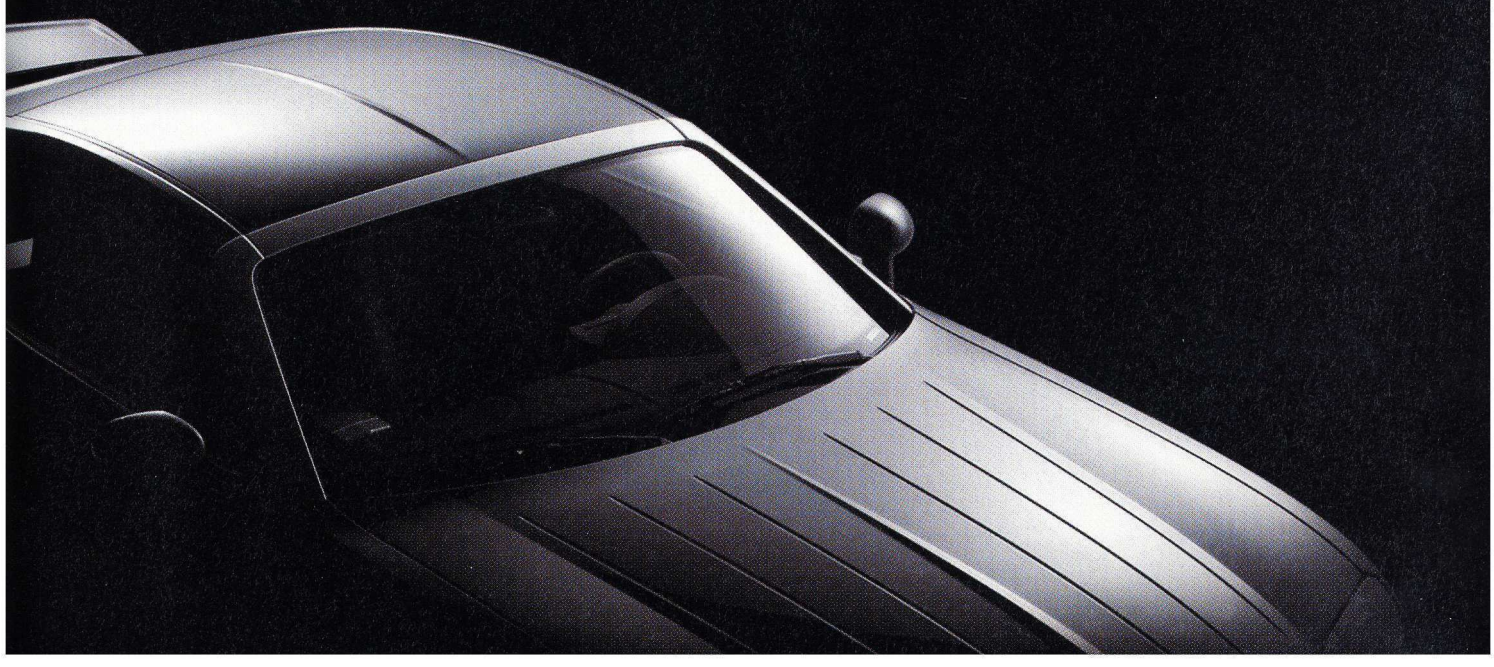

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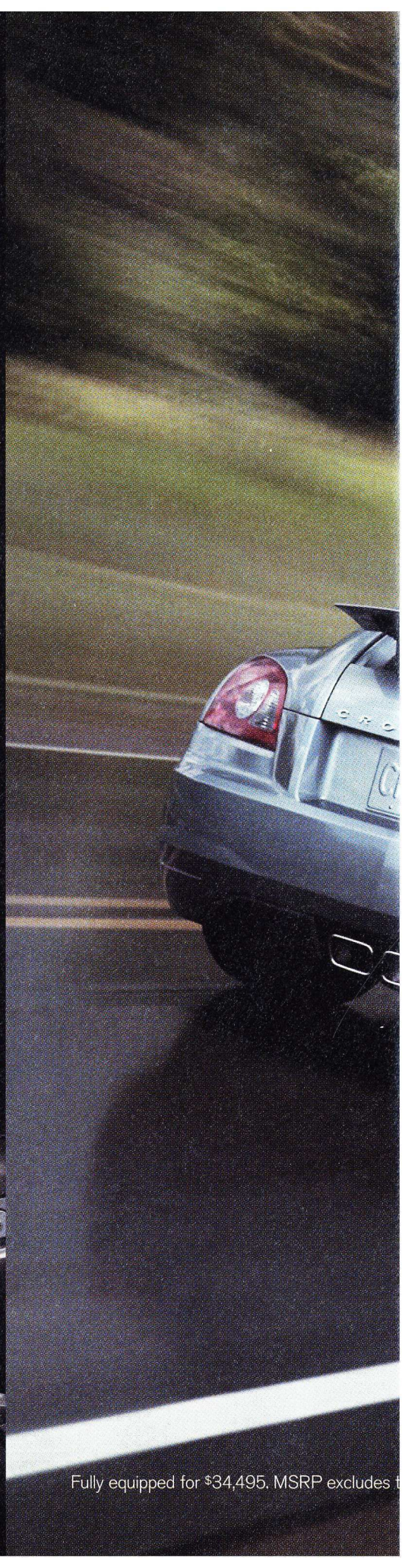

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Biotech+ Medicine

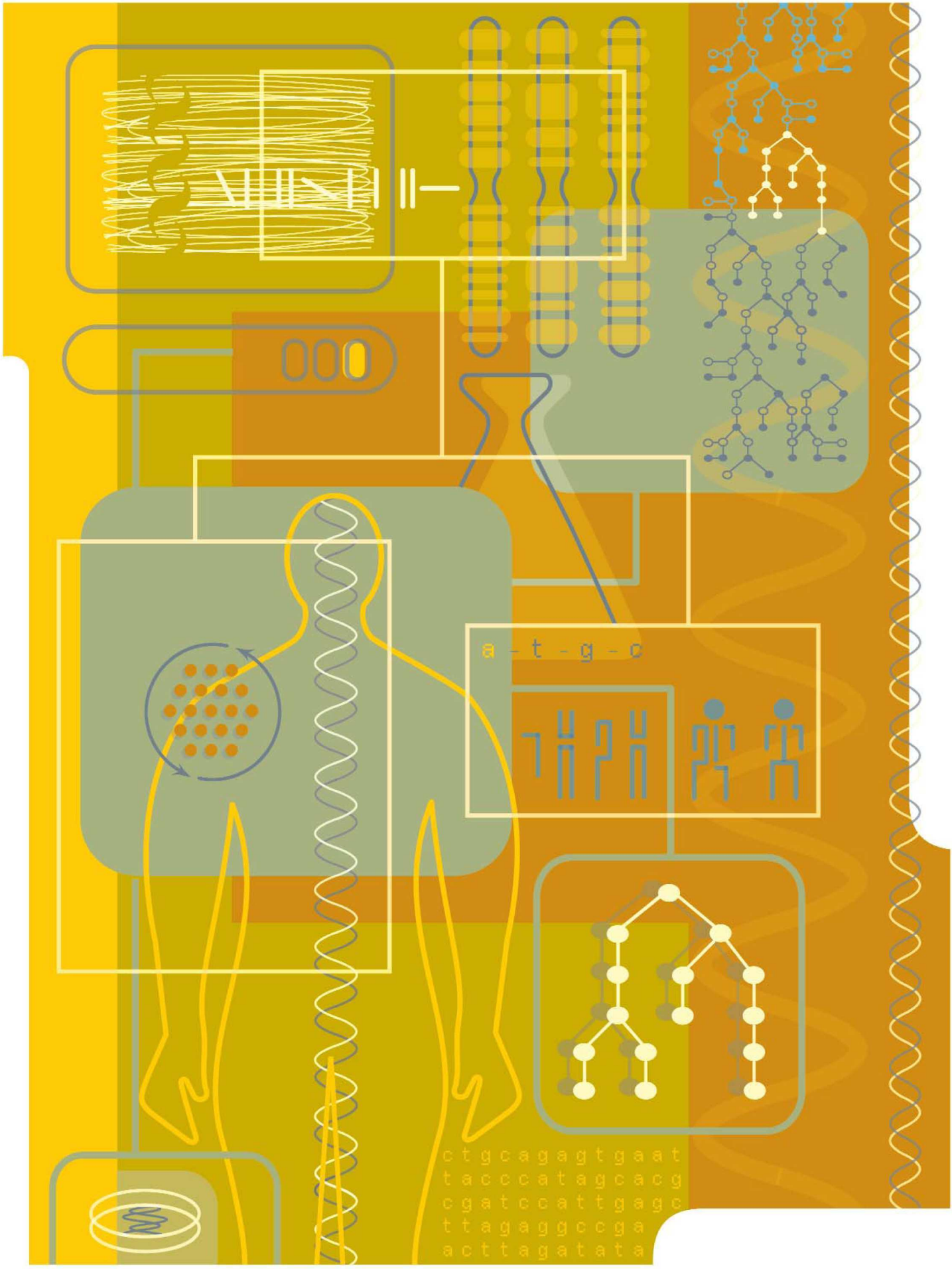
The convergence of biology with computing and nanotechnology is yielding safer and more effective medicines.

IN THE WORLD of biomedical research, basic science is usually held in the highest regard, while applied research is often looked down upon as mere "tool building." But don't tell that to this year's TR100 honorees in biotechnology and medicine, a group intent on turning recent biomedical advances into practical technologies with an immediate impact. ■ These researchers and entrepreneurs work in wildly divergent fields, from nanoengineering to "programming" living cells. Not surprisingly, they hold a range of opinions on which approaches and developments in biology are the most important and on how new technologies will affect our lives. Yet they share a desire to find real-life applications for their technologies as soon as possible. They also share an awareness that the convergence of biology and medicine with fields such as physics, engineering, computer science, materials science, and nanotechnology is yielding powerful new ways to help them achieve their ambitions.

Take **Eugene Chan**. Even as an undergraduate at Harvard University, Chan was intrigued by the Human Genome Project, the international effort to determine our genetic blueprint. But Chan also appreciated that the project's true promise would only be realized when the technology was available to obtain full genetic information on individuals—prohibitively expensive and time consuming with the sequencing methods used in the Human Genome Project. "With all these wonderful [genetic] discoveries in the past 50 years, it's now time to translate that from a research basis to a practical reality for each and every one of us," Chan says. To usher in that reality, Chan quit medical school and founded Woburn, MA-based U.S. Genomics. He hired biologists, physicists, nanotechnologists, and informaticists, each of whom plays a role in realizing his vision: a machine capable of reading an entire human genome in 10 minutes.

That ambition to improve lives characterizes many of the TR100. Rice University bioengineer **Jennifer West** says that making a difference to patients is "one of the nicest things to see." West is developing new materials for both treating cancer and engineering replacement tissues in the body. West and her colleagues at Rice found that by attaching particular proteins to tiny, hollow gold nanoparticles, called nanoshells, they could selectively target and destroy tumor cells. As a cofounder of Houston-based Nanospectra Biosciences, West is now helping to develop the nanoshells for cancer therapy. Here's how it might work: A doctor injects the materials intravenously and waits an hour for the nanoparticles to find the cancerous cells. When the doctor shines infrared light on

BY ERIKA JONIETZ » ILLUSTRATION BY CELIA JOHNSON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the patient, the nanoshells heat up and destroy only the tumor tissue. West believes that interdisciplinary research like hers, which combines advances in biology, medicine, and nanotechnology, will yield tremendous opportunities to create new treatments. "That's where a lot of the successes will come from," she says.

The juncture of biology and computer science is another promising area of convergence. Princeton University electrical engineer **Ron Weiss** is undertaking the ambitious task of "programming" living cells, encoding instructions using genes rather than the *1*s and *0*s he used when programming computers. As a postdoc at MIT, Weiss was looking to biology to inspire new methods of computer programming. "At some point I said, 'Instead of just staring at things on the screen, I really want to program cells.'" He hopes soon to begin programming tissue-specific human stem cells, instructing them on how to become different types of cells and, eventually, whole organs.

Weiss also foresees ultrarealistic computational simulations of cells or even humans that will be able to predict precisely what will happen as environmental conditions change or as foods or medicines are consumed. "Once we have that predictive power, that's the point where progress is really going to increase," he says.

Such dramatic dissolution of the boundaries between biology and computer science will take years. But other frontiers have already blurred enough to yield new technologies unimaginable a short time ago—such as **Nimmi Ramanujam**'s optical method of cancer diagnosis. The University of Wisconsin-Madison biomedical engineer studies how light interacts with human tissue and the characteristic changes cancers introduce to those interactions. Her efforts have yielded a noninvasive test for cervical cancer that is already in human trials. She's now working on a breast cancer test that could be an aid to expensive and often inaccurate breast biopsies. The goal, she says, is to develop methods that can identify cancer at its earliest stages with very high accuracy and in real time—which would be a boon to thousands of cancer patients.

Pioneering work like Ramanujam's is only the beginning of the transformation the TR100 honorees believe the accelerating pace of biomedical discovery will yield. Such rapid increases in knowledge, coupled with the new tools resulting from advances in areas such as nanotechnology and computer science, have led some in the TR100 to confidently predict that a "golden age" in biological science is emerging. "As we're getting more and more information from things like genomics and proteomics, we're gaining the ability to manipulate biology and do lots of new and exciting things with it," says West. "Up to this point, we just didn't know enough to understand how to make these things happen." Armed with the new technologies and this new knowledge, the researchers you'll meet in the next few pages are now intent on making their ambitious goals happen.

TR100 Startups in Biotech and Medicine

INNOVATOR	COMPANY FOUNDED/COFOUNDED	STRATEGY/ MILESTONES
Alexis Borisy	CombinatoRx (Boston, MA)	New medicines generated by combining drugs; drugs for cancer and rheumatoid arthritis in human trials; has raised $60 million
Eugene Chan	U.S. Genomics (Woburn, MA)	Technology to rapidly sequence genomes; has raised more than $57 million
Bassil Dahiyat	Xencor (Monrovia, CA)	Computational protein drug design; human trials of anti-inflammatory drug scheduled for late 2004; has raised $65 million
Benjamin G. Davis	Glycoform (Oxford, England)	Novel drug delivery systems based on carbohydrate chemistry; has raised $2 million
Christophe Echeverri	Cenix BioScience (Dresden, Germany)	Drug discovery using RNA interference technology; has raised 11 million euros working with corporate and academic partners to identify genetic targets for new drugs
Michael E. Gertner	Nanomedical Technologies (San Francisco, CA)	Drug delivery systems using nanometer-sized pores in metallic films that can release medicine in devices such as artery-supporting stents over longer periods than standard polymer coatings
Jay Groves	Synamem (formerly Proteomic Systems) (Burlingame, CA)	Drug discovery using "MembraneChip" technology
Andre Koltermann	Direvo Biotech (Cologne, Germany)	"Directed evolution" to make novel proteins and enzymes for more effective drugs, detergents, and food products; has raised more than $25 million
Anthony Lowman	Gelifex (Philadelphia, PA)	Hydrogel implants to relieve pain and restore motion in cases of degenerative back disc disease
Gavin MacBeath	Merrimack Pharmaceuticals (Cambridge, MA)	Drug discovery using systems biology approaches to understand complex pathways; drug for myasthenia gravis in human trials; has raised $25 million in investments
Christophe Schilling	Genomatica (San Diego, CA)	Computational models of cells that enable biologists to engineer organisms to produce valuable chemicals; $3 million in venture funding
Mijail Serruya	Cyberkinetics (Foxborough, MA)	Brain-computer interfaces to allow paralyzed patients to communicate or control robotic aids, and to treat epilepsy and depression; has raised $9.3 million
Micah Siegel	Concept2Company (Palo Alto, CA)	Support for university researchers who wish to start commercial ventures in medical devices, life sciences, and information technology without leaving their current jobs
Jennifer West	Nanospectra Biosciences (Houston, TX)	Hollow gold nanoparticles coated with proteins for targeted cancer therapy
Daphne Zohar	PureTech Ventures (Boston, MA)	Venture creation; helps found and fund life sciences companies


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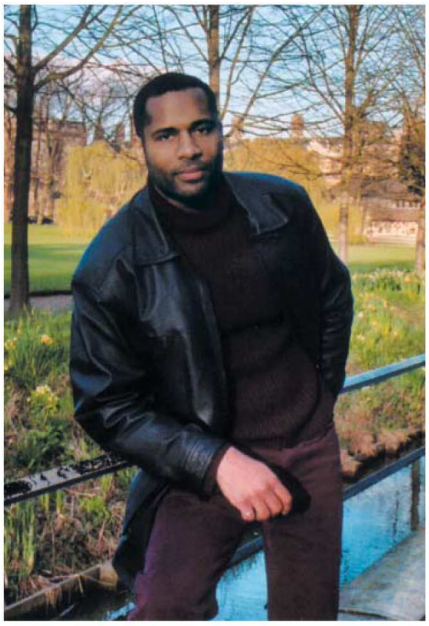

Guillermo Ameer, 33

Northwestern University

Synthesized "biorubbers" that could replace damaged heart and lung tissue and rebuild blood vessels

GUILLERMO AMEER is creating a set of high-tech tools to manage diverse medical conditions. "Most people in science tend to focus on one specific problem," says the biomedical engineer, a native of Panama. His aim is broader: "I want to build things useful to people's health." His top tool to date is called biorubber: a rubber-band-like material that he helped invent during a postdoctoral fellowship. Stretchy, cheap, and biodegradable, biorubber could eventually be used to replace damaged heart or lung tissues. Ameer's lab at Northwestern University is currently developing second-generation biorubbers with varying degrees of elasticity and degradation rates to act as scaffolds for engineered blood vessels or ligaments. While the assistant professor of biomedical engineering has two patents pending on that work, he has already received a patent for another innovation: a cartridge that uses genetically engineered antibodies to filter a protein called beta-2-microglobulin from the blood of kidney disease patients. Over time, this protein—which the traditional filters in dialysis machines don't catch—can leave painful deposits in bones, joints, and tendons. Partly funded by the National Kidney Foundation and Baxter Healthcare, Ameer's lab is refining the biofilter so clinical trials may be conducted—which means people could soon find out just how useful Ameer's tools are.

Helene Andersson, 29

Silex Microsystems

Produces portable, inexpensive, microprocessor-size labs for research and industry

WITH TWO degrees and three part-time jobs, Helene Andersson is bridging disciplines to build and market microprocessor-size laboratories. At Stockholm, Sweden-based startup Silex Microsystems, she serves as business manager and designs custom "labs-on-a-chip" for commercial uses ranging from bedside medical testing to detecting chemical and biological attacks. And the electrical engineer and molecular biotechnologist is exploring other applications in her work at Sweden's Royal Institute of Technology and at Mesa+, a research institute in the Netherlands. As a doctoral student, Andersson developed production techniques for efficiently manufacturing the microlabs, and designed ever smaller pumps, valves, and other components for them. Several of her patented microstructures "boldly demonstrate to bioanalytical researchers the great advantages of microlabs," says Mesa+ professor Albert van den Berg. These advantages include portability, speed, and economy. Andersson's life is hectic, but she plans to continue all her pursuits. "It suits me very well," she says, "to explore new things and learn how to do business with them at the same time."

Sangeeta Bhatia, 35

University of California, San Diego

Uses microchip-manufacturing tools to build artificial livers

IN THE United States alone, 17,000 people await liver transplants. Sangeeta Bhatia's solution? Engineer a liver from scratch, using photopatterning techniques borrowed from the microchip industry. A completely functional artificial liver requires different types of cells arranged in complex patterns. The University of California, San Diego, associate professor of bioengineering and associate adjunct professor of medicine starts by mixing one type of liver cell with a liquid polymer and covering the mixture with a template. When ultraviolet light shines through the template, illuminated cells get trapped in the polymer; shaded cells can be washed away. By applying different templates and cell mixtures, Bhatia builds up layers that simulate the liver's natural structure. Human trials remain years away, but meanwhile biotech firm Surface Logix is adapting her liver-cell work for drug research.

Alexis Borisy, 31

CombinatoRx

Believes that combining different drugs could yield better ways to fight disease

FOR DECADES, "drug discovery" has meant screening millions of compounds to find one that will block a disease process. But Alexis Borisy says that approach is too simplistic. Since "the body always uses mixtures of molecules to regulate itself," he says, it makes sense to do the same when treating disease. In 2000 Borisy founded CombinatoRx in Boston to search for molecules already proven safe for humans but that combat disease only when used in combination. Along the way, he had to reinvent drug screening. While pharmaceutical companies typically ask only one question about each compound—does it have an effect?—CombinatoRx examines compounds two at a time, in different doses, answering that question 36 separate times. Borisy says the company had to create new lab processes and write software to analyze its masses of data. CombinatoRx has raised $60 million and has launched human trials of three drug combinations designed to treat cancer and rheumatoid arthritis. "Fifty years from now," Borisy says, "a majority of drugs will be combination by design."


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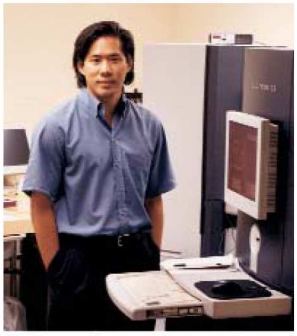


Eugene Chan, 29

U.S. Genomics

Aims to speed genome sequencing with a machine that reads DNA letter by letter

MOST BIOTECH firms have their origins in labs, but Eugene Chan dreamed up U.S. Genomics in the medical-school dorms and libraries of Harvard University. His goal: to find a quicker, cheaper, more precise way to analyze DNA so all patients might benefit from the discoveries of the Human Genome Project. Chan patented his idea for a device that would read a DNA sequence straight from a single molecule—and left medical school in his second year to found U.S. Genomics in Woburn, MA, to develop the technology. The company's latest prototypes catch fluorescence-tagged DNA on nanoscopic posts, unfurling the coiled molecules. The molecules then flow one by one into a narrow channel where lasers and optical detectors "read" the bar-code-like patterns created by the tags. The device can now identify certain sequences within long stretches of DNA; Chan hopes it will produce letter-by-letter sequences by 2006. He has raised some $57 million and recruited such sequencing gurus as Celera Genomics founder J. Craig Venter to the firm's board. "The machines he's built probably have hundreds of different applications," Venter says.

Bassil Dahiyat, 32

Xencor

Designs proteins from scratch to create new medicines

AS AN undergraduate studying biomedical engineering, Bassil Dahiyat planned a career building medical devices. Pursuing a PhD at Caltech, however, he found himself working on much smaller structures: proteins. Indeed, Dahiyat designed the first completely artificial protein—a very simple one—by devising powerful algorithms that combine standard descriptions of the physical properties of protein molecules in novel ways. He then constructed the protein by chemically linking its amino acid building blocks. After

graduating in 1997, Dahiyat founded Xencor and put his technology to work creating protein drugs. The Monrovia, CA, company has raised $65 million and plans next year to begin human trials of its first drug, an anti-inflammatory for treatment of rheumatoid arthritis, psoriasis, and Crohn's disease. Today Xencor designs its drug candidates by "tweaking natural proteins," says CEO Dahiyat, but he looks forward to computer models robust enough that he can design complex molecules from scratch, fulfilling his vision of completely artificial protein therapies. "The dream is to mimic how nature uses proteins—to essentially do any task you can imagine," he says. "There's this palette that we haven't even started to paint with."

Christophe Echeverri, 34

Cenix BioScience

Develops fast, automated processes for figuring out genes' functions

WHEN SCIENTISTS discovered that short pieces of RNA can shut down specific genes—a phenomenon called "RNA interference"—they hailed the finding as "revolutionary." As a postdoc in 1998, Christophe Echeverri co-led the first group to successfully test the use of RNA interference to shut down genes selectively across an entire genome. Such an approach could prove crucial to determining what the tens of thousands of genes in animal and human genomes actually do. Scientists had devised a few RNA-based methods for determining gene function, but they were too time-consuming to stride through a full genome, sometimes taking months to analyze a single gene. Echeverri helped lead a team that developed micromachinery, chemical reactions, and algorithms to automate the process and record its outcome. Echeverri says his team uncovered the roles of four to six genes per day. The triumph prompted Canadian-born Echeverri to cofound Dresden, Germany-based Cenix BioScience in 1999; the 35-employee company has raised 11 million euros. In partnership with Austin, TX, biotech firm Ambion, Cenix is developing the first commercially available human-genome-wide libraries of interfering RNA molecules, which clients could use to find new drug targets.

Benjamin G. Davis, 33

Glycoform

Manipulates biological sugars for more precise drug delivery

RESEARCHERS HAVE long known that proteins—pivotal players in everything from embryonic development to Alzheimer's disease—often have sugars attached to them. But understanding precisely how those sugars influence the proteins' functions was exceedingly difficult until the arrival of novel chemical reactions devised by University of Toronto postdoc Benjamin Davis. The reactions enabled Davis to add or substitute sugars on proteins with Lego-like ease—solving a problem that had stymied researchers for decades. Manipulating sugars could make it easier not only to systematically study the basic biology of proteins, but also to engineer them as drugs. Indeed, Davis is exploiting his techniques to create a drug delivery system in which different sugars direct protein-based drugs to target cells or organs. In November 2002, Davis, who is now a lecturer at the University of Oxford, cofounded Glycoform in England to commercialize this and other work; within a week he obtained $2 million in venture funding. The company is now conducting trials of the drug delivery system and developing new sugar attachment techniques.

JOHN SOARES (CHAN)

Michael E. Gertner, 33

University of California, San Francisco

Set out to improve the tiny devices that keep once blocked arteries open

WHEN MICHAEL Gertner is convinced he's right, it's damn the torpedoes, full speed ahead! A resident in general surgery at the University of California, San Francisco, Medical Center, Gertner pondered how to improve coatings for stents—tiny expandable structures that doctors implant to help hold coronary arteries open once they have been unblocked by angioplasty. Each year, more than 900,000 coronary stents are deployed in the U.S., and over time they can become covered with scar tissue that can once again impede blood flow. New stents are coated with polymers that, for a week or two, release a drug that inhibits scarring, but the polymers can degrade the drugs or even harm blood vessels. Gertner reasoned that a metal coating could work better. Ignoring some experts who doubted his approach's commercial viability, he and a colleague developed a process for coating stents with metallic films. The metal forms a fine lattice that carries drug molecules it can release for up to six months. Although surgery keeps Gertner busy, he has cofounded Nanomedical Technologies in San Francisco to develop the system. A stent manufacturer has already acquired parts of the technology. Time will tell if those doubting experts were wrong.

Jay Groves, 32

University of California, Berkeley

Patented a lab-on-a-chip to investigate cell proteins that cause disease

FOR JAY Groves, inspiration began with tweezers. As a graduate student, Groves was studying cell membranes—the fatty wrappers that enclose living cells—and the proteins that stud them. Though 80 percent of drugs work by binding to these proteins, they are poorly understood and hard to study. While trying to measure the motion of cell membrane proteins, Groves scratched the silica surface supporting them with his tweezers to help focus his microscope. He noticed that the molecules couldn't move across the scratch—and a new idea was born. Could researchers create patterns on wafers that would, like the scratch, corral proteins? Sure enough, Groves developed and patented the MembraneChip, a silica surface etched with tiny squares that partition cell membrane proteins so they can be studied. In 2000 he launched a five-person biotech company, Proteomic Systems, now called Synamem, in Burlingame, CA, which licensed the MembraneChip to seek new drugs that suppress immune response or fight infection. Groves, who is now an assistant professor of chemistry at the University of California, Berkeley, says the technology could affect the study of autoimmune diseases, among other disorders. "Membranes are the definitive structural feature of life," Groves says—and he is determined to master their ways.

Justin Hanes, 34

Johns Hopkins University

Creates systems for delivering drugs to where they're needed in the body

AFTER LOSING his grandmother to cancer when he was 10, Justin Hanes vowed to combat disease. Now a chemical engineer, he has already won his first battle, designing polymer aerosols that deliver drugs to the lungs. Inhaling medications spares patients from injections, and certain drugs are more effective when breathed in. Hanes and his coworkers devised a way to make coated polymer particles porous; the particles serve as drug-carrying vessels that are large enough to lower the odds of attack by the immune system, but light enough to stay aloft and reach deep into the lungs. There the polymer degrades, releasing insulin, growth hormones, or asthma medication over hours, days, or weeks. Hanes and his colleagues' pioneering work provided the core technology for Advanced Inhalation Research, founded in Cambridge, MA, in 1997 and sold two years later for $114 million. Although Hanes received stock from the sale, he chose an academic career. Now an assistant professor at Johns Hopkins University, he is building a new polymer for transporting cancer drugs. Enzymes secreted by growing tumors destroy the new polymer, thus discharging drugs where they're needed most. "Why spread poison over the whole yard to eliminate one weed?" Hanes asks.

WILL KIRK (HANES)

Andre Koltermann, 34

Direvo Biotech

Speeds protein evolution to improve detergents, medicines, and foods

AN ADMIRER of Charles Darwin, Andre Koltermann is bent on speeding up natural evolution. Bacteria, for example, produce enzymes with useful stain-fighting properties, but nature has yet to make an enzyme that performs optimally alongside the harsh chemicals in laundry detergents. Andre Koltermann says his company, Direvo Biotech, has. Koltermann and his colleagues have altered an enzyme used in commercial detergents, making it a hundred times more effective at eliminating stains. They did so by adapting "directed evolution," a technique for inducing the genes that encode the enzymes to mutate or recombine. Researchers use fluorescence spectroscopy to screen for promising variations. The process enabled Koltermann to find the best enzymes more quickly than is possible with conventional techniques. Founded in Cologne, Germany, in 2000 by Koltermann and two partners, Direvo has secured more than $25 million in financing. Koltermann will use the funds to expand the firm's work in directed evolution, with the aim of improving the enzymes in medicines, foods, and animal feeds.

Erin Lavik, 30

Yale University

Helped paralyzed rats walk again and aims to do the same for people

A PLAYWRIGHT who has written a one-act farce, Erin Lavik has a day job that is no laughing matter. She uses polymers and neural stem cells to promote recovery from spinal-cord injuries, which 10,000 people suffer each year in the United States alone. A Yale University assistant professor of biomedical engineering, Lavik designed polymer scaffolds that mimic the architecture of a healthy spinal cord, seeded the scaffolds with neural stem cells, and implanted them in paralyzed rats. Much to everyone's surprise, the rats were able to move their limbs, bear weight, and even walk. Although spinal-cord-injury research is a big field, Lavik's method is the first to demonstrate such dramatic success. Repairing spinal-cord injuries in humans will be a bigger challenge, but then, Lavik didn't expect her injured rats to walk so soon. If she has her way, people with spinal-cord injuries could be walking sooner than expected, too.

Xiangjun Liu, 35

Tsinghua University

Maps gene variations that could warn of future disease

MOLECULAR BIOLOGIST Xiangjun Liu wants to know whether something in your genes can predict your likelihood of contracting a debilitating disease. The human genome contains many small person-to-person variations called single-nucleotide polymorphisms (SNPs). SNPs are associated with a variety of diseases, but defining which combination of SNPs can predict the onset of a specific disease is a formidable task. As a researcher at Celera Genomics in Rockville, MD, Liu laid the groundwork for that effort by leading a team that sifted through billions of genetic sequences and produced a database of 2.8 million SNPs. Researchers worldwide are using these data to learn which genetic variations are involved in diseases and how those variations might affect drug efficacy and toxicity in different people. In February 2002 Liu returned to his native China to advance this work as director of Tsinghua University's Bioinformatics Research Lab in Beijing. The lab is trying to pinpoint the SNPs associated with atherosclerosis and other ailments. Liu also heads a Chinese government project to analyze SNP findings worldwide. Ultimately, Liu hopes to identify people likely to develop a given disease, so doctors can work proactively to prescribe treatments that will prevent or minimize symptoms.

Gavin MacBeath, 33

Harvard University

Unravels complex biological systems in his search for new drugs

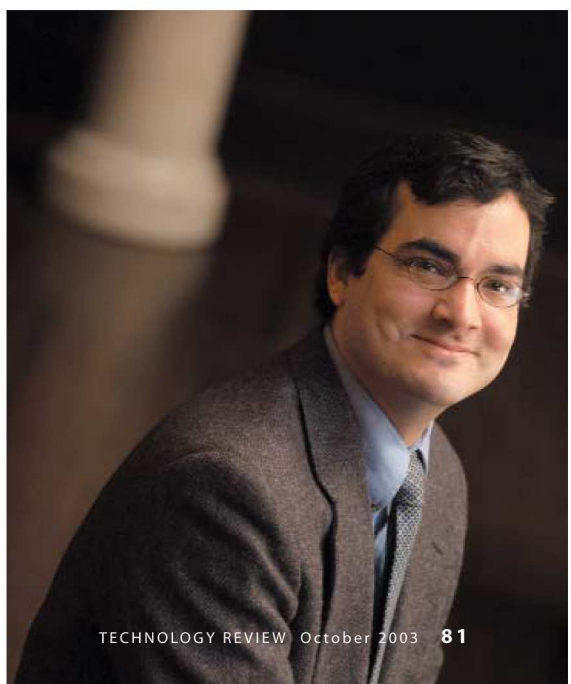
BIOLOGISTS TRADITIONALLY study organisms one gene or one protein at a time. But because organisms are collections of interwoven systems that involve interactions of many molecules, more and more researchers believe a systems-level approach to biology is critical for understanding diseases and developing cures. Gavin MacBeath is working on technology to facilitate that approach. An assistant professor in Harvard University's chemistry and chemical biology department, MacBeath has found a way to attach thousands of functional protein samples to small glass chips. Using these chips, he can study more than 25,000 interactions between pairs of proteins in a single afternoon. He also plans to look for small molecules that can selectively disrupt interactions—both to learn more about basic biology and to identify potential drugs. In 2000, MacBeath cofounded Merrimack Pharmaceuticals in Cambridge, MA, to use systems biology to improve research on afflictions such as cancer. "This kind of work is going to change the way we discover drugs," he says.

Anthony Lowman, 33

Drexel University

Packs insulin into gel pills that could replace injections for diabetes patients

AS A graduate student, Anthony Lowman faced a dilemma: pursue polymers or medicine. He chose both. Now a chemical engineering professor at Drexel University, Lowman specializes in hydrogels—versatile blends of gelatinous particles and water. Certain medications, such as insulin, cannot be taken orally because enzymes in the stomach break them down before they can be absorbed into the bloodstream. Lowman created a novel way of shielding insulin inside polymer-based hydrogels. The hydrogels have pores that can hold insulin and open only in response to the high pH of the upper small intestine; there, the insulin diffuses into surrounding tissue. The technology, now in animal testing, could enable patients with type 1 diabetes (more than a million in the United States) to take insulin-filled gel pills in lieu of injections. Lowman is researching a similar approach to delivering drugs for cancer, osteoporosis, and other conditions. In his part-time job as chief technical officer for Gelifex, a Philadelphia-based company he cofounded in 2002, Lowman is designing injectable hydrogels for repairing degenerative discs, the cause of back pain in five million Americans. He recently prepared a gel that could restore disc pressure and function. Clinical trials may begin in late 2004.



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Heather Jakes is happy. SCHOTT's entry into Biochips has taken off at a record pace. New research labs were built in record time and coated glass substrates for DNA chips were developed with equal speed. Hardly surprising:
y it's all about being fast. But
nough for SCHOTT. In pharmaceutical research the development at top speed is highly valued. In fact the next big breakthrough is just around the corner: biochip technology platforms. With more innovations to follow. Right, Heather?
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Nimmi Ramanujam, 35

University of Wisconsin-Madison

Uses light to help make diagnosing breast and cervical cancer faster, more accurate, and less invasive

DO I have cancer? Is my unborn child in trouble? University of Wisconsin-Madison biomedical engineer Nimmi Ramanujam believes that the millions of women who face these questions each year deserve more accurate answers than those afforded by today's diagnostic technologies. Consider breast biopsies. Doctors sometimes miss the tumor cells they're trying to sample, so Ramanujam has developed a device that can help guide a biopsy needle to just the right spot. An optical fiber threaded through the needle shines light of different wavelengths on cells at the needle's tip; molecules in cancer cells respond by fluorescing in characteristic ways, and sensors register the fluorescence. Ramanujam and her colleagues are already testing the technology in patients undergoing breast cancer surgery and plan to test it in patients undergoing breast biopsy within the next year. A cervical-cancer detector she began developing as a graduate student uses a similar approach; it is now in large-scale human trials. Ramanujam is also harnessing light to noninvasively monitor how well oxygen is getting to fetuses, an important—and currently unmeasurable—indicator of when emergency cesarean sections are needed. With Ramanujam's help, those babies will be born into a world where medical questions get better answers.

Shuvo Roy, 33

Cleveland Clinic Foundation

Builds tiny machines that can warn of impending heart attack and monitor healing after surgery

AS A graduate student, Shuvo Roy developed microelectromechanical systems (MEMS)—tiny machines like sensors and actuators—for airplane and rocket engines. He had an aerospace job lined up, but inspired by his father, a public-health physician, he wanted to "impact people's lives more directly." The Bangladesh native switched career paths in 1998, cofounding a laboratory at Ohio's Cleveland Clinic Foundation devoted to clinical applications of MEMS. Roy's efforts have yielded several innovative devices and one patent—with seven others pending. Among his inventions is a wireless strain and pressure microsensor that can be inserted into vertebrae during spinal-fusion surgery (a main surgical option for back patients) to monitor bone fusion. Additionally, Roy shrunk ultrasound imaging technology into a high-resolution transducer small enough to glide through arteries on a catheter; the device can spot arterial defects called vulnerable plaques, considered the leading cause of heart attacks. Roy also developed durable silicon membranes that could replace short-lived polymers as blood filters in dialysis machines—a step toward creating implantable artificial kidneys. "Shuvo doesn't care about recognition," says lab codirector Aaron Fleischman. "He just wants to get technology that can help people into the hands of doctors."

Ram Samudrala, 31

University of Washington

Wrote algorithms that can predict the functions of proteins from the sequence of a genome

SINCE BEFORE University of Washington assistant professor Ram Samudrala was born, scientists have been striving to predict from an organism's DNA sequence the identities and workings of its many proteins. Such an understanding could lead to improved treatments for diseases, which are often caused by malfunctioning proteins. Samudrala has advanced that effort by producing algorithms that can predict the structure and function of every protein encoded by an organism's genome. By modeling changes to specific genes or proteins, researchers can try to determine what causes proteins to go awry. One set of algorithms Samudrala devised, with $4 million from federal and private agencies, is called Bioverse. Samudrala has used Bioverse to model the functions and interactions of the proteins of more than 30 organisms; other researchers are using Bioverse to find which proteins in pathogens would be good targets for new drugs. Posted on the Web, Bioverse receives 1,000 hits daily. Samudrala made the algorithms free because he is opposed to intellectual-property restrictions, as explained in his "Free Music Philosophy" statement, which he published on the Web in 1994—long before the rise of Napster.

Christophe Schilling, 29

Genomatica

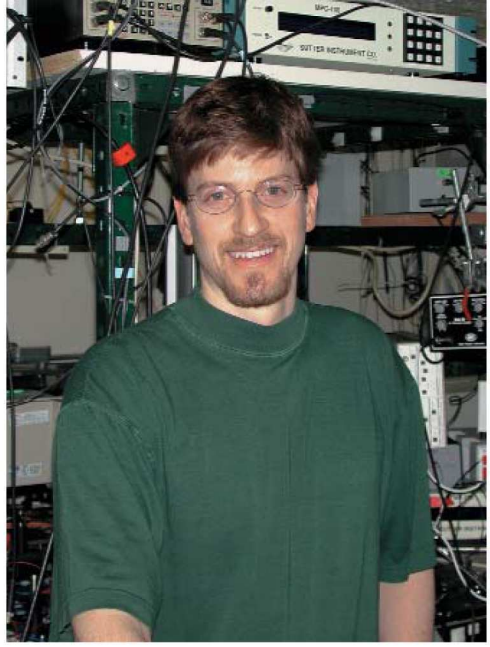
Transforms microbes into fine-tuned manufacturing machines

WHEN HE was just 26, bioengineer Christophe Schilling won a small-business grant from the National Science Foundation. His plan was to reengineer the genomes of microorganisms such as bacteria and yeast, which are used as living chemical factories, to produce new or better products. With his university mentor, Bernhard Palsson, Schilling raised $3 million to launch Genomatica in San Diego in 2000. Today, the company is attracting partners such as Dow Chemical that want to engineer microbes to churn out chemicals used to make everything from drugs to soaps. Although that goal is not unique, Genomatica's tool is: software dubbed SimPheny that decodes a microorganism's genome data into a "parts list" of molecular components and enables the construction of computer models of the microbe's metabolism. Corporate clients can then tap the models to predict a particular organism's industrial potential. Genomatica also plans to release the software to select university labs by 2004.

Mark Schnitzer, 33

Stanford University

Sheds light on the functioning of individual brain cells



BY COMBINING physics, neuroscience, and optics, Mark Schnitzer intends to directly observe single neurons deep below the surface of the living mammalian brain; it would be a scientific first. While working at Lucent Technologies' Bell Labs, Schnitzer crafted an incredibly small endoscope—a fiber-optic viewing device with lenses as small as 350 micrometers across. The scope illuminates brain cells that have been labeled with a fluorescent dye; detectors in the device pick up the fluorescence and software constructs images of the cells. The device could allow neuroscientists to see how brain cells function, grow, and communicate across tiny synaptic gaps. Already, researchers are preparing to use Schnitzer's tool to study how animals store long-term memories. Because it is so small, the endoscope could also be fed deep into the brain, inflicting minimal harm on surrounding neurons. Human trials are years away, but Schnitzer says eventually his tool may help doctors detect brain cancers and blood clots without biopsy. Now an assistant professor in Stanford University's departments of applied physics and biological sciences, Schnitzer continues to apply his tools to brain research.

Micah Siegel, 33

Concept2Company

Transforms research from universities and national labs into successful startups

THOMAS EDISON and Eli Whitney are Micah Siegel's idols—not just because they were great inventors, but because they turned their inventions into revolutionary products. "Ninety percent of the rewards go to the guy who figures out how to scale up what he is doing," says Siegel. He earned PhDs in electrical engineering and molecular biology at Caltech, where he codeveloped genetically engineered sensors that change colors whenever a neuron's functions are excited or inhibited. Twenty pharmaceutical labs are now using the sensors to test drugs. Business success excited Siegel's own neurons, so in 2000 he cofounded Concept2Company in Palo Alto, CA, to help other scientists commercialize research. Since then, he has evaluated more than 350 business proposals from university and national labs and has raised millions of dollars of investments in several startups. In some deals, C2C steps in and handles the "business functions" many scientists hate—attracting management teams, licensing patents, schmoozing customers, raising capital—improving researchers' chances of becoming Edisons or Whitneys.

Mijail Serruya, 29

Cyberkinetics

Connects brains directly to computers in the hope of helping paralyzed people communicate and control robotic aids

IT TAKES incredible patience to interview people so severely paralyzed they can communicate only with the blink of an eye or the twitch of a brow. But it was partly impatience that inspired Mijail Serruya to do just that. The Brown University medical student and PhD was helping to develop a "brain-machine interface," and he was eager to put it to work helping profoundly disabled people. Talking to them about their needs was an important step. Brain-machine interfaces could potentially allow paralyzed people to communicate through computers and to control robotic wheelchairs and aids. Serruya started by fine-tuning algorithms that allow signals recorded by electrode arrays implanted in the brain to change the position of a cursor on a computer screen. He says his colleagues were planning to explore human applications "one day," but to him the question was, What are they waiting for? Aiming to move the interface into human trials, Serruya, Brown neuroscientist John Donoghue, and two others founded Foxborough, MA-based Cyberkinetics in 2001. They have hurdles to clear before they can begin human tests, Serruya says, but one gets the sense that all they need is a little patience.

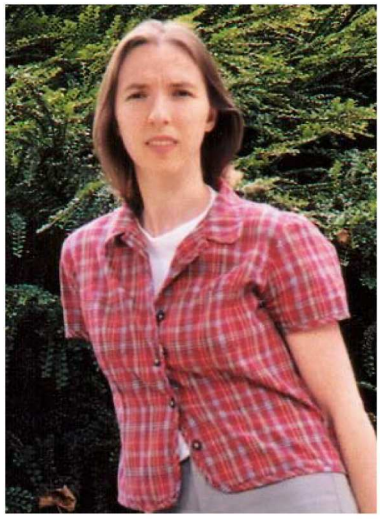
Giovanni Traverso, 27

Johns Hopkins University

Came up with a noninvasive alternative to colonoscopy

A COLONOSCOPY is the best way to diagnose colon cancer, but it's so inconvenient and unpleasant that less than 25 percent of the at-risk population ever have one. The main alternative, a test for traces of blood in a stool sample, generates a high percentage of false positives. So Giovanni Traverso, a staff researcher at Johns Hopkins University's Kimmel Cancer Center, set out to develop a convenient gene-based stool test that would reliably detect colon cancer at its earliest stages—when it's still curable. Traverso had to develop sophisticated methods for isolating minute amounts of relevant DNA from feces samples patients collect at home, as well as a novel means of finding cancer-causing mutations in the DNA. In an early study, the test generated no false positives, but it didn't detect all cancers. Traverso and colleagues are working to automate the test and boost its sensitivity; he's also about to resume medical school in England. With luck, as a doctor, he'll be able to get patients to take a colon cancer test that could save their lives.

A. ATEMASOV (SIEGEL); JOHN ABROMOWSKI (SERRUYA)



Rita Vanbever, 33

Catholic University of Louvain

Wants to make treating diabetes as easy as breathing

DRUG FIRMS are vying to create the first inhaled version of insulin, which could deliver therapy more simply and effectively than needles to millions of diabetics. Rita Vanbever's work might give Eli Lilly the edge. An associate professor of pharmaceutical technology at the Catholic University of Louvain in Belgium, Vanbever provided much of the chemical expertise that led to low-toxicity porous aerosol particles that carry insulin deep into the lungs. The particles do not clump, as earlier, smaller and denser particles did, and they can be used with both fast-acting and long-acting drugs. Cambridge, MA, drug firm Alkermes has licensed Vanbever's techniques and is using them in partnership with Eli Lilly to develop inhaled human growth hormone in addition to insulin. Barriers remain; Vanbever discovered that human immune cells known as macrophages in the lung's air sacs prevent up to 50 percent of such protein therapeutics from being absorbed into the bloodstream. But she is confident that her delivery methods will ultimately shrink that percentage significantly.

Jennifer West, 32

Rice University

Synthesizes blood vessels that could reduce the trauma of heart surgery

EVERY YEAR more than 500,000 U.S. residents undergo coronary-artery bypass surgery. Soon, thanks to Rice University associate professor of bioengineering Jennifer West, that procedure may be less painful. To create a bypass, doctors must harvest a blood vessel—usually from the patient's leg. West, however, is growing vessels in the lab. She starts by synthesizing polymers that contain biological signaling molecules, the same molecules that guide tissue growth in the body. She molds the synthetic polymers into a blood-vessel-shaped template that is then seeded with three different types of live cells; by optimizing the polymers for different cell types in different regions of the template, she can recreate the architecture of a natural vessel. The signaling molecules direct the cells to form new tissue, and the polymer support degrades in response. Human tests of the technology could start in five to 10 years, West says. Meanwhile, other heart patients might benefit from another West innovation: a polymer that could be used to coat an artery after angioplasty to prevent new blockages from forming. And West's innovations address more than heart disease. She cofounded Nanospectra Biosciences in Houston to develop a cancer therapy based on gold nanoparticles that destroy tumor cells.

Ron Weiss, 33

Princeton University

Programs living cells to sense toxins or create replacement tissues

RON WEISS likes to give orders. In his lab at Princeton University, the assistant professor of electrical engineering sets the conversation and dictates the action. His charges, however, are not students but cells. Weiss builds synthetic DNA circuits—strings of genes that operate much like the logic circuits of computers—and injects them into *E. coli* bacteria, where they direct cell behavior. His goal? Create networks of different cells that work together to sense environmental toxins, generate new tissue, or perform other jobs. Collaborating with researchers at Princeton and Caltech, Weiss shares almost $6 million in grants, much of it from the U.S. Defense Advanced Research Projects Agency. In one of his projects, Weiss leads a multiple-laboratory effort to program groups of cells to act as biological sentinels. Such systems could detect and pinpoint the locations of anthrax or other biological weapons. In another project, Weiss is devising faster, more reliable ways to direct stem cells to create new tissues to replace those lost to disease or injury—which means that one day a doctor might be able to order your own cells to heal you.

Daphne Zohar, 33

PureTech Ventures

Spots promising biotech work and helps build new companies to commercialize it

DAPHNE ZOHAR is a serial entrepreneur who is comfortable moving into almost any niche. She began by launching a successful olive oil brand. Then she pitched her patented "hoofpad"—basically, a sneaker for racehorses—to veterinarians. Today she is forging biotech startups. The daughter of a Massachusetts General Hospital researcher, Zohar grew up around labs and has become good at recognizing commercial potential in lab work that might be otherwise unexplored. She is founder and CEO of Boston-based PureTech Ventures, which evaluates 15 ideas a week and chooses three each year to build businesses around. "Being an entrepreneur is like solving a puzzle with most of the pieces missing," she says. PureTech's stable includes companies making chips that rapidly analyze proteins, ultrasensitive antibody tests to screen blood banks for infectious agents, and nanoscale drug delivery systems targeting lymph nodes to treat cancer and HIV. Zohar's team and advisors at PureTech include former Pharmacia and Upjohn CEO John Zabriskie and financier Todd Dagres of Battery Ventures, which manages $1.8 billion in capital. "I look for vision, determination, and entrepreneurial spirit," Dagres says. "Daphne possesses all those traits."

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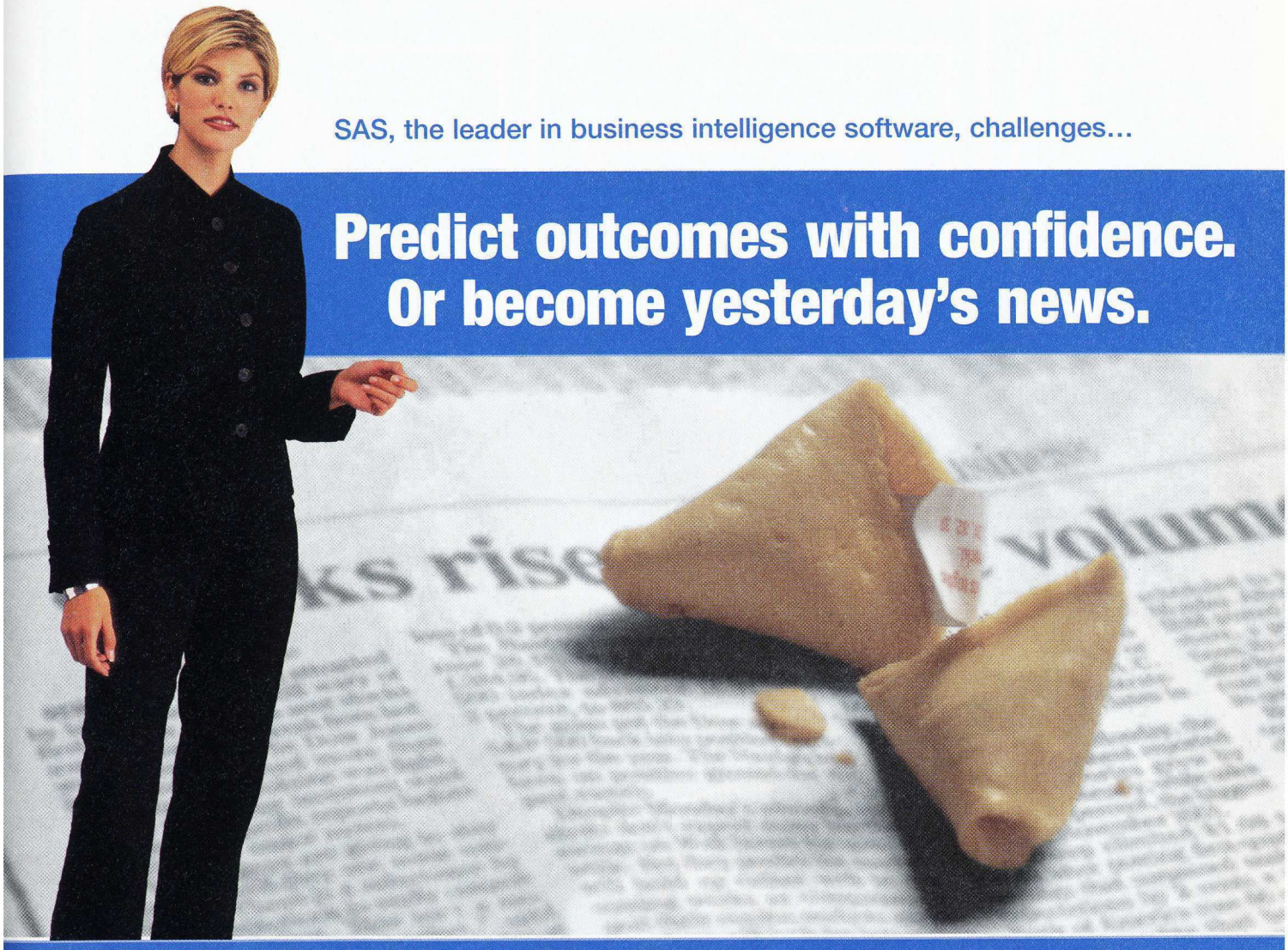

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Internet

Smarter networks and a boom in wireless sensors will change how you use and think about the Internet.

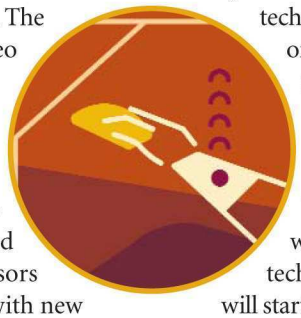
FOR THE PAST two years, the telecommunications industry meltdown that some equipment makers referred to as a "nuclear winter" has left plenty of people concerned about the future of communications networks—and even of the Internet itself. Despite the downturn, however, the TR100 honorees in the Internet category share an optimistic outlook on the next generation of technologies and services. ■ This year's honorees point to the recent widespread adoption of 802.11 wireless data networks and the expected growth of voice transmission over the Internet as fundamental changes that will make both data and voice services ubiquitous properties of all networks. That—along with the anticipated expansion of the market for inexpensive wireless sensors—will permit far smarter networks in which authority for controlling data is distributed among appliances and servers that analyze and share information on traffic patterns, even predicting user needs to activate additional capacity in advance. Taken together, these technologies will help transform how and why the Internet is used and provide plenty of opportunities for the industry to revive itself.

"Instead of having a high-speed backbone and one point in your home for Internet access," says **Jason Hill** of JLH Labs, a Capistrano Beach, CA, startup he founded, "it will be a more fluid system with highly distributed access." To help make that happen, Hill has developed an operating system for small wireless sensors that permits them to establish contact with one another and share data. In the next three years, says Hill, a whole new generation of inexpensive sensors a few millimeters in size will be designed and integrated into our surroundings—and even into the fabric of clothes. Following on the heels of this first wave of sensors will be a communications infrastructure to take advantage of all of these new data collection points. Hill says the collective intelligence of these sensors will offer greater flexibility than the centralized scheme of today's telecom infrastructure. With more information collected at various endpoints on the network, better data will be spread evenly throughout the infrastructure—allowing network operators to make more accurate decisions on how to route traffic and respond to outages.

During its boom years, the Internet acquired many of the characteristics of a broadcast medium; a few large Web sites claimed a big portion of online traffic. But recent developments seem to be reversing this trend. Several TR100 innovators point to the phenomenon of Web logs, or blogs, as a first step in creating greater opportunity for consumers to view and use all kinds

BY LEE BRUNO » ILLUSTRATION BY CELIA JOHNSON

of new digital media—including not just text but also still images and video. "Today, content for the Internet is produced by very few and viewed by many," says **John Apostolopoulos**, senior researcher at Hewlett-Packard's streaming-media-systems group in Palo Alto, CA. To improve users' ability to share digital content, Apostolopoulos, who has done pioneering work on video compression for high-definition television, is working on coding schemes for sending video data to a given recipient along several different pathways simultaneously. Large video files could thus be ferried across the network without loss of quality. The work will eventually permit broader use of video across both the Internet and telecom networks.



Extending the reach of the Web is raising the expectations of both business users and consumers. One of those expectations is smarter networks whose parts have greater autonomy to respond to changes, without the intervention of centralized servers. Similarly decentralized networks of sensors and appliances will permit people to experiment with new forms of communication. Web connections could allow the remote control of everyday appliances like thermostats, lighting fixtures, and other systems in homes and businesses.

And there will be plenty of surprises ahead in how people interact with these smarter networks. New uses as unexpected as blogs were will likely emerge. "People will live their lives in public in ways they've never done before," says **Martin Wattenberg**, research staff member at IBM in Cambridge, MA. "People like to tell stories around the campfire, and blogs are kind of similar," he says. "It is a very human way to present information." For his part, Wattenberg is developing data visualization tools so that people can better navigate communications channels and sort through the enormous trove of information that results.

With this shift in both the overall volume of digital content and the number of people producing it, there will also be a push for stronger security to protect its use and distribution. And that push points back to the more intelligent infrastructure that handles, stores, and forwards data packets to customers and businesses. Once the first elements of the intelligent-networking infrastructure and security mechanisms are in place, which should happen in about three years, businesses will be better able to protect digital data like video and images. This will enable the wider use of the Internet for such distribution chores as delivering new films to theaters. AT&T's **Lorrie Cranor** is designing technology that will help provide the needed privacy for online interactions. Cranor is working on the Platform for Privacy Preferences Project (P3P); browsers using P3P permit users to keep better tabs on whether their personal data are being surreptitiously hijacked.

Smarter, more adaptable networks, which are both aware of and adapt to users' needs, will take a while to fully emerge, says **Jennifer Yates**, principal technical staff member at AT&T. But elements of them will start to show up in the Internet's main data pipelines and gradually work their way out to end users. Innovations in these networks will help Internet service providers anticipate user needs and activate additional services tailored to changing traffic demands. For example, Yates says, an intelligent network will automatically supply additional bandwidth to video presentations; it will then revert to a less pricey speed for basic data transfer.

For the most part, microprocessors and PCs have become commodities distinguishable only by price, believes **Jud Bowman**, who founded Pinpoint Networks to help companies distribute data applications to wireless devices. That means software and services, not new hardware, will usher in the truly disruptive innovations within the emerging wireless data infrastructure. In the following pages you will meet many of those who are bringing about these changes—and reviving hope in the moribund telecom and Internet businesses. TR

TR100 Startups in the Internet and Telecommunications

INNOVATOR	COMPANY FOUNDED/COFOUNDED	STRATEGY/MILESTONES
Brian Behlendorf	CollabNet (Brisbane, CA)	Software tools to improve the productivity of teams collaborating over the Internet; recently announced Sony as a customer; raised $13 million in private funding last January
Jud Bowman	Pinpoint Networks (Durham, NC)	Tools to help telecom operators manage applications and improve service quality; has raised $20 million in venture financing
Jason Hill	Dust (Berkeley, CA)	Low-cost wireless sensors with built-in networking logic to share data
	JLH Labs (Capistrano Beach, CA)	Wireless sensor network operating systems
Meg Hourihan	Pyra Labs (San Francisco, CA)	The software (Blogger) that made Web logging the online rage; acquired in February 2003 by Google (Mountain View, CA)
Paul Meyer	Voxiva (Washington, DC)	Technologies to convey public-health information over either the Web or touch-tone phones; has raised $5.6 million in private investment
Sanjay Parekh	Digital Envoy (Norcross, GA)	Software to identify the geographic location of Web site visitors for improved customer service or customized content; has raised $12 million from AOL Time Warner Ventures and others
Reuben Singh	alldayPA (Manchester, England)	Outsourced administrative support for small-business owners; also operates the Golden Fund, a $24 million war chest to help struggling tech companies
Andrew Wheeler	Ember (Boston, MA)	Wireless sensors and networking software for the automation of buildings, factories, utilities, and battlefield operations; has raised $28 million in venture financing
Evan Williams	Pyra Labs (San Francisco, CA)	See Hourihan, above

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John Apostolopoulos, 35

Hewlett-Packard

Develops ways to improve the security of streaming video on the Net

THE ONLY TR100 innovator who can also say he's an Emmy Award winner is John Apostolopoulos. As an MIT graduate student, he helped develop the video compression system that was integrated into the U.S. Digital TV standard for high-definition television, for which he received a Technical Emmy in 1997. That year Apostolopoulos joined Hewlett-Packard Laboratories, aiming to improve the fidelity and security of streaming video—video sent through the Internet in continuous flows of data packets. The Internet is vulnerable to errors, or even attacks, that can keep those packets from their destinations, so Apostolopoulos designed a technique for sending video information across multiple paths simultaneously rather than relying on a single path. Interruption of one path doesn't kill the transmission because the missing video can be recovered using the stream from another path. Meanwhile, a security-conscious U.S. government agency, which Apostolopoulos prefers not to identify, is evaluating a method he codeveloped for encrypting media streams so they can be carried by diverse networks and then adapted for viewing on diverse devices. Now a senior research scientist, Apostolopoulos has begun to tackle streaming-media schemes for wireless networks.

Brian Behlendorf, 30

CollabNet

Sparked the widespread development of Web servers, mainstreaming the nascent Web

FEW PEOPLE have had as broad an impact on the Web's development as Brian Behlendorf. In 1993, while an undergraduate at the University of California, Berkeley, Behlendorf set up wired.com, one of the earliest nonacademic Web sites. In 1994 he led the team that built hotwired.com, the first ad-supported site. That same year, Behlendorf contributed to the development of the Virtual Reality Modeling Language, which added animation, music, and video to what had been a text-laden Web. But Behlendorf's most important contribution came in 1995 when he founded the Apache Web Server Project, which sparked the proliferation of university and commercial server computers. Apache is a freely available, Unix-based Web server program that is now used to host more than 65 percent of the world's Web sites; it is unquestionably one of the most important open-source projects in the history of computing. The Apache Software Foundation, which Behlendorf led for three years, now has 700 developers working on 120 projects to improve the Web. In 1999 Behlendorf founded CollabNet, a software firm in Brisbane, CA, that offers Web collaboration tools to help companies write software more efficiently.

Jud Bowman, 22

Pinpoint Networks

Wrote software that is accelerating the expansion of wireless networking

STEVE NELSON, a venture capitalist and chairman of Durham, NC-based Pinpoint Networks, says Jud Bowman "gains knowledge in the morning that becomes great business judgment in the afternoon." Bowman exercises that judgment as Pinpoint's founder and CEO. In 1999 Bowman deferred undergraduate admission to Stanford University to launch Pinpoint with a high-school friend. The company's initial offering was a search engine that helped cell-phone users find wireless-data applications such as instant-messaging software. But Bowman quickly recognized that incompatibilities among handsets and service providers were stymieing wireless networking. So Pinpoint created Fuel—a software platform that acts as a mediator, feeding wireless applications from just about any network to just about any handset. Bowman believes Fuel could accelerate the wireless market; he's raised $20 million in capital and has licensed Fuel to cellular giants Verizon Wireless and U.K.-based mmO2. Fuel faces fierce competition from rival startups, telecommunications companies, and handset makers, but Bowman shows little strain, finding time to play viola in the Raleigh (NC) Symphony Orchestra. He never did find time for college.

Lorrie Cranor, 32

AT&T

Leads the global effort to improve privacy practices and tools on the Web

IN HIGH school, the artistic Lorrie Cranor had no interest in a computer career, but today she is chair of the World Wide Web Consortium's Platform for Privacy Preferences Project (P3P). P3P, a high-profile collection of Internet protocols released in 2002, has been adopted by more than 500 companies and will soon be added to more than 400 U.S. government sites. It allows Web sites to produce machine-readable privacy statements free of legal jargon, and enables browsers to interrogate these privacy policies automatically whenever they access Web pages. Both the Netscape and Internet Explorer browsers have adopted P3P and take it a step further by blocking third-party cookies—those files Web sites plant on visitors' hard drives to send back data. Discussion of P3P's specifications began within the consortium in 1997, and Cranor, a leader in privacy research at AT&T who holds a doctorate of science in engineering and policy, steered representatives from industry, government, and academia toward consensus.

Jason Hill, 26

JLH Labs

Wrote software that allows hundreds of minute wireless sensors to communicate better

WHEN SANDSTORMS raged during the 2003 Iraq war, coalition forces stalled because they could not track enemy movement. Small wireless sensors scattered across terrain could in principle do the tracking instead—and Jason Hill, a PhD in electrical engineering and computer science, has created free software called TinyOS that greatly reduces the cost of setting up and running such a sensor network. Sensors in previous networks relayed information about acoustic vibrations or magnetic fields along predetermined paths to base stations. TinyOS allows the sensors to pass messages to any nearby peer as needed. The system can survive if some sensors are destroyed and reduces reliance on costly base stations, making for quicker deployment and greater flexibility. Today, 80 companies, including Intel and Bosch, use TinyOS in everything from military surveillance to energy monitoring. Last year Hill cofounded Dust in Berkeley, CA, to build custom network applications, some already sold to Honeywell to help grocery stores monitor power usage, and he has now started his own firm, JLH Labs in Capistrano Beach, CA.

Meg Hourihan, 31

The Lafayette Project

Sparked the rise of the popular Web-based journals known as blogs

MEG HOURIHAN didn't intend to start a revolution when she cofounded the San Francisco Web application company Pyra Labs with fellow TR100 honoree Evan Williams *(see p. 97)* in 1999. The duo, along with programmer Paul Bausch, created the pioneering application Blogger. Web logs, or "blogs," are frequently updated, Web-based journals kept by individuals or groups; they have become wildly popular, with people around the globe now posting Web links, political commentary, or even diaries on them. Before Blogger, one had to be fluent in the HTML code—and rent server space—in order to put up a Web log. Blogger removed this barrier with a simple interface that allows anyone to create a Web log, hosted free on Pyra's servers. Today, Blogger has more than one million registered users. After leaving Pyra Labs in 2001, Hourihan cofounded the Lafayette Project in New York City, where she directs development of a Web-based search tool to help manage the growing glut of blogs. Last February, Pyra Labs was bought by search engine giant Google, where Blogger and its servers live on.

Paul Q. Judge, 26

CipherTrust

Wrote software that stops spam and viruses before they enter a network

WHERE MOST of us see a nuisance, Paul Judge sees a security threat. While working on his master's thesis on secure content distribution, Judge became employee number four at CipherTrust, an Atlanta data security startup. Judge, now chief technology officer, envisioned a black box installed at the gateway between the Internet and a corporate or campus network that would block unwanted e-mail and viruses before they slowed productivity or destroyed data. Leading a team of 10 developers (all older than he was), Judge produced IronMail, a computer that runs a series of spam filters and virus detectors, some based on algorithms the team created. Now deployed at 700 corporations and universities, IronMail stops 95 to 98 percent of incoming spam without blocking legitimate mail, Judge says. He also founded the Spam Archive, a research storehouse of junk e-mail, and his efforts led to his appointment as the first head of the Anti-Spam Research Group within the Internet Research Task Force, a professional society. "Over the years, the anti-spam community has focused on symptom relief," Judge remarks. "The Anti-Spam Research Group was formed to focus on a cure."

SCOTT JULLIFF (JUDGE)

Rasmus Lerdorf, 34

Yahoo!

Invented a server language that brought live data to the Web

BORN NEAR the North Pole on Greenland's Disco Island, Rasmus Lerdorf has learned five languages while living around the world. But it's the language he invented that has had global impact. In 1995, without any formal programming training, Lerdorf developed a server language to help him set up Web sites he was designing for companies. He named the language PHP, for PHP hypertext preprocessor—an acronym that contains itself. Once embedded in the Web's basic addressing protocol, PHP solved a fundamental problem. Before PHP, Web pages were dominated by static text and pictures; creating sites that could readily incorporate up-to-date information or interact with databases was difficult. PHP made all that possible. Lerdorf offered his code free, and today companies worldwide, including Ericsson, CBS, and Yahoo!, use it as the backbone for more than 12 million sites, where it enables live financial data, news feeds, and stock tickers. Along the way, Lerdorf worked stints at IBM and Linuxcare. In September 2002, he joined Yahoo! to assist it in migrating to PHP-based tools, a move expected to speed development and reduce training costs.

Lih Y. Lin, 34

University of Washington

Built micromirror switches for faster, all-optical telecommunications networks

AT ABOUT three times the diameter of a human hair, the micromechanical optical switches that Lih Lin designed for AT&T in 1997 and 1998 were scarcely visible. And the minuscule machines she subsequently built solved a fundamental problem in telecommunications. Information travels at high speed over the optical fibers that form the backbones of telecom networks, but converting the optical signals to electronic bits for processing by traditional circuitry limits the network's overall transmission rate and increases its cost. Lin introduced pivoting micromirrors that can switch light-wave signals directly, circumventing the pitfalls of electronic manipulation. Her technique has since been widely developed and is enhancing the capacity and reducing the cost of the optical-fiber network, as well as enabling faster and broader-band data and video transmission over the Internet. Lin's work has yielded 16 patents and 120 published papers. As a newly appointed associate professor of electrical engineering at the University of Washington in Seattle, she plans to apply her knowledge of photonics and micromechanics to biotechnology to devise new kinds of imaging tools that can analyze individual cells.

Paul Meyer, 33

Voxiva

Brings database and Web-like services to remote areas through touch-tone phones

THERE ARE about 2.5 billion phones worldwide but only 600 million computers. Knowing this, Paul Meyer, a Yale Law School grad and former speechwriter for President Clinton, founded Washington, DC-based Voxiva in 2001 to help isolated communities access computing power through touch-tone telephones. Because phone use requires neither literacy nor much electricity, the system benefits regions that are short on both. Launched with funding from the Markle Foundation and the World Bank, Voxiva enables users to input and retrieve information by tapping phone buttons, listening to messages, and speaking responses. In Peru, health-care workers can call a Voxiva server to submit reports about patient symptoms or disease outbreaks. Peru's Ministry of Health has already collected 50,000 reports on threatening diseases. Meyer's ingenuity has benefited other countries as well. Working with the International Rescue Committee in 1999, he built a wireless network that became Kosovo's first Internet service provider. He also set up a Lotus Notes system to help reunite refugees in Guinea. Impressed with Voxiva's performance, the U.S. government hired the company to track the effect of smallpox vaccinations on U.S. soldiers.

Sanjay Parekh, 29

Digital Envoy

Develops software that lets companies tailor services to their customers' locations

STUCK BEHIND a dial-up connection in 1999, Sanjay Parekh grew frustrated having to enter information like his city and state before he could find store locations on, say, the Federal Express and Ikea Web sites. "These sites should already know where I am," he thought. Rather than curse at his monitor, he formed Digital Envoy in Norcross, GA, to make his idea real. Four years later his product, NetAcuity, is used by eBay, AOL Time Warner, Microsoft, and others to determine a visitor's locality. It traces connections back through Internet switching stations to the network nodes where log-ons originate—almost always in a visitor's city or town. This is close enough to give users local weather forecasts, or the addresses of nearby electronics stores, without their having to enter any data. NetAcuity also enables Web sites to automatically tailor advertisements. A billboard ad for Home Depot, for example, could announce a sale at a store near the visitor's home. Indeed, Google uses NetAcuity to target area-specific ads. "A lot of people don't know about us," Parekh says, "but everyone is touched by us."

Reuben Singh, 27

alldayPA

Provides support services and startup money for entrepreneurs

REUBEN SINGH combines technology and capital to help other entrepreneurs. He started his first business—a fashion accessories shop—at age 18, and four years later, as CEO of a retail chain, he was worth millions. Relying heavily on eight assistants, he realized that most other time-strapped entrepreneurs could use the same kind of support. So in 1999, he used $6 million of his own money to found alldayPA in Manchester, England. The company uses custom software that enables a team of live personal assistants to handle calls, manage calendars, type letters, and perform other tasks for business owners, whose customers need never know that the assistants are at a 650-seat around-the-clock call center. AlldayPA now has a database of 94,000 registered customers, who save money by not having to hire employees. Meantime, Singh's Golden Fund, a $24 million war chest for acquiring and turning around ailing information technology companies, has aided more than a dozen businesses. The Bentley-driving CEO is helping other entrepreneurs through Dream On Attitude, a venture capital fund that invests his and other people's cash in startups founded by innovators younger than 25.

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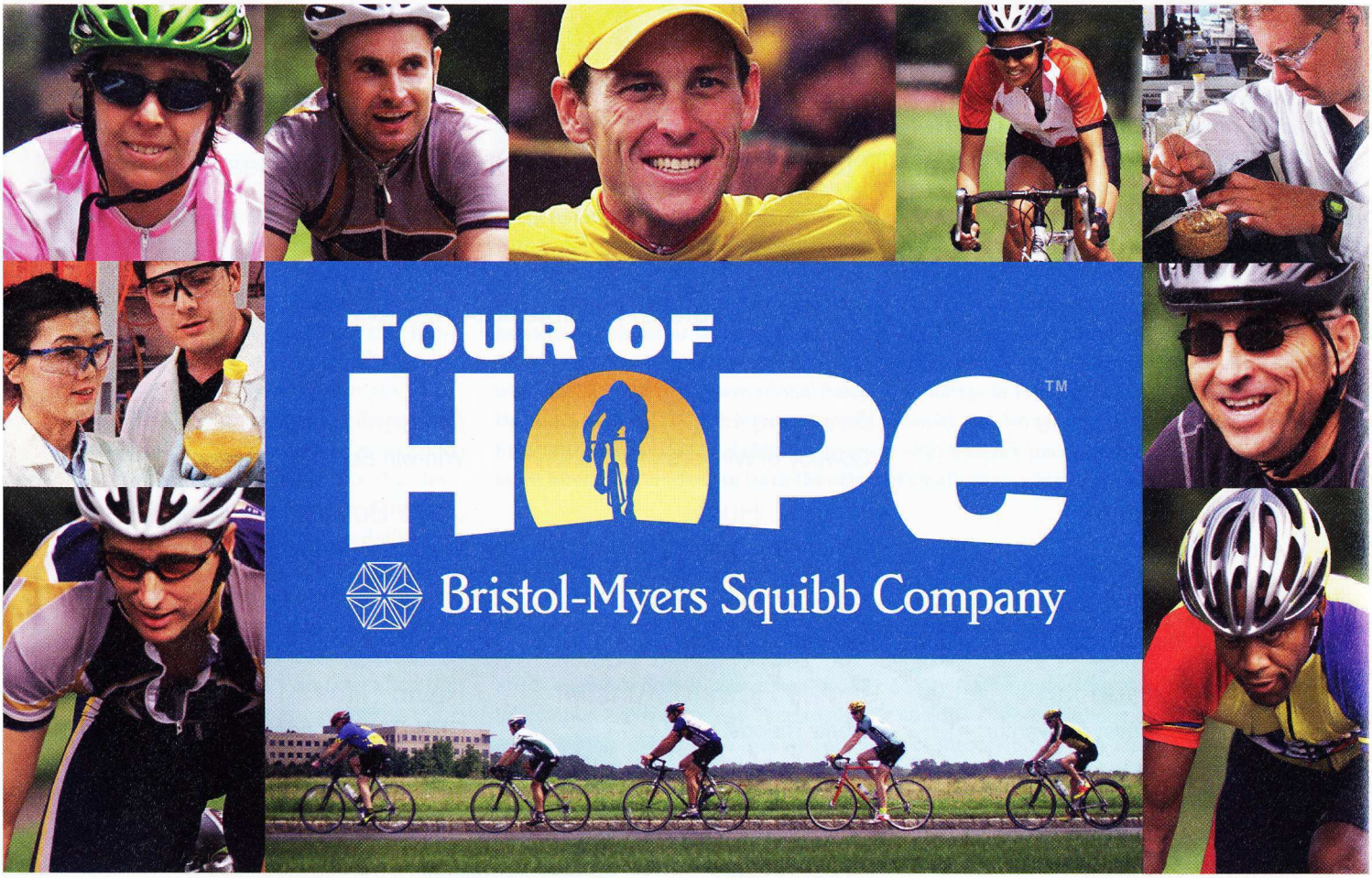

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Andrew Wheeler, 24

Ember

Builds wireless sensor networks that improve industrial efficiency

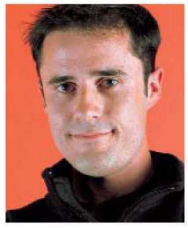
FROM HAWAII to Norway to Japan, Andrew Wheeler's wireless sensor networks are providing real-time control over factory conditions, energy usage, and inventory. As a graduate student at MIT, Wheeler built small processors with built-in sensors and radios that could be spread around a factory or power plant, where they organized themselves into smart communications networks that could manage sensor information, such as temperature. Wheeler's hardware and data-routing algorithm proved reliable in field tests, so in 2001, he cofounded Ember in Boston, one of the first companies to commercialize self-organizing nodes for wireless sensing and control. An intensely curious engineer who can "focus like a battering ram," in the words of Michael Hawley, his advisor at MIT, Wheeler helped raise $28 million for Ember in a difficult investment climate—which has enabled the company to aggressively sell its communications nodes to customers in industry, to utility companies, and to defense contractors.

Martin Wattenberg, 32

IBM

Simplifies people's electronic lives with graphical data management

BY THE time he completed his first high-school calculus class, Martin Wattenberg had already coauthored a software package for teaching calculus using a more visual method. Since then he has employed his rare combination of mathematical and artistic talent (New York's Whitney Museum of American Art has exhibited his computer-based art) to introduce new ways of visualizing data. At SmartMoney.com, his popular, Java-based, interactive "Map of the Market" offers investors color-coded graphical representations of market capitalization and stock activity for more than 500 companies. Rather than sifting through reams of data, investors can monitor the map for real-time color changes indicating whether a stock is up or down. His current research for the Collaborative User Experience group at IBM focuses on creating a visual paradigm for electronic collaboration. One tool under development will present users with maps of their in-boxes that highlight the names of people they owe mail to and can graphically trace the history of each message. Wattenberg's innovations at IBM are still in the lab (he only joined the company last year), but his skills should help people better organize and make sense of their increasingly electronic existence.



Evan Williams, 31

Google

Fueled the expansion of blogs across the Web

EVAN WILLIAMS is a survivor. In early 2001 he was the sole remaining employee of Pyra Labs, the San Francisco company he had cofounded with fellow TR100 honoree Meg Hourihan ***(see p. 93)*** **and programmer Paul Bausch. They had designed Blogger, a Web application that allows people to create Web logs (or "blogs")—Web pages where users can maintain Internet journals. Blogger helped realize the promise of the Internet: that ordinary folks with no programming experience could use it to air their views. Blogger's friendly interface—and free server space—are widely popular. After the dot-com crash, when Williams had trouble raising money to buy badly needed servers, Pyra Labs asked users for help, and they donated more than $10,000. That modest infusion was enough for the company to rally, and Blogger's popularity skyrocketed. It currently has more than one million registered users. Williams continues to develop Blogger at search engine heavyweight Google, which bought Pyra Labs last February. He believes blogs will become "an accepted part of the media ecosystem." Indeed, blogs have turned public attention to overlooked news, including the controversial remarks of Trent Lott (R-Mississippi) that led to his ouster as U.S. Senate majority leader.**

Jennifer Yates, 31

AT&T

Wrote software widely adopted by the telecom industry that speeds up optical networks

AS A graduate student, Jennifer Yates was the only optical-network researcher in her native Australia. In 1999 she took a job in the United States at AT&T, where she went about rethinking the conventional method for managing optical networks, which required expensive hardware; Yates created an architecture, based on the common Internet Protocol, that uses software employed at each network node to do the same job. Previously, manual processes and centralized management computers set up each network connection and switch individually, slowing communications and introducing bottlenecks. Instead, Yates's software is deployed across the network. Because the software can establish new connections and restore broken ones quickly, it lowers capacity demands and eliminates congestion. This network management method is now being adopted by the telecommunications industry as the General Multi-Protocol Label Switching standard, embraced today by behemoths such as Lucent Technologies and Tellium.

ASIA KEPKA (WHEELER)

Nanotech

New materials engineered on the nanometer scale will lead to commercial products for electronics, energy, and medicine in three to five years.

ASK STEPHEN EMPEDOCLES, director of business development at Nanosys in Palo Alto, CA, to sum up the state of the emerging nanotechnology market, and he'll say, "confusion." Today there are thousands of academic nanotech groups and more than a hundred companies that have "nano" in their names. Yet aside from a few odd items like stain-free pants and supercharged tennis balls that tout their nano ingredients, there are still few if any significant commercial products based on nanotechnology. That could be about to change. ■ This year's TR100 honorees in the category "nanotech and more," which includes materials, energy, and transportation, work in areas as diverse as electronics, fuel cells, and traffic modeling. But it is nanotech that is getting the most attention these days, and within that growing discipline, the focus of the TR100 is clearly on transforming laboratory curiosities into real commercial technologies.

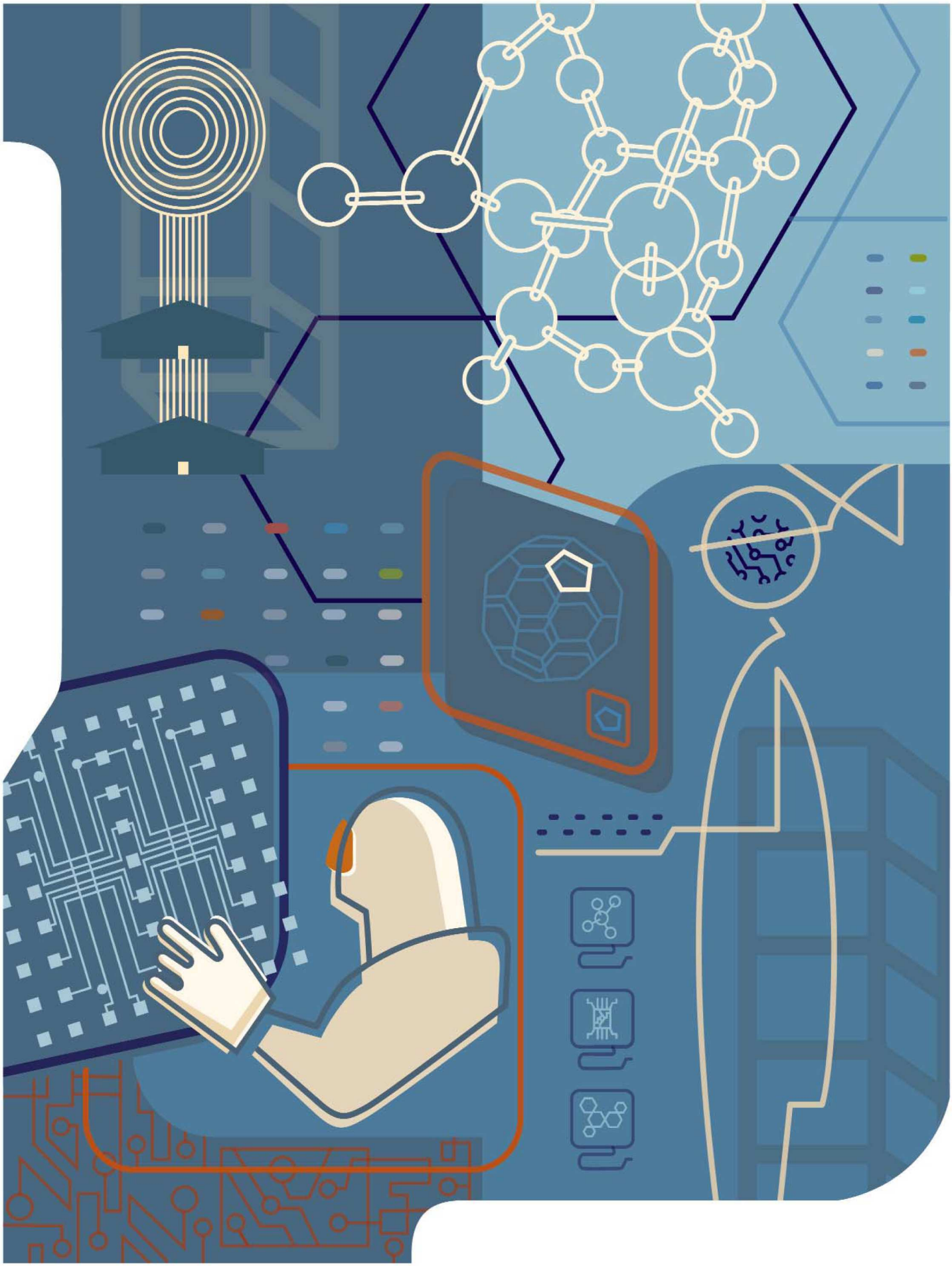
If they succeed, mass-produced nano-based materials will soon be used to build devices that will reconfigure existing markets in areas as diverse as energy, medicine, and computing. "We need to show the world that in fact nanotech isn't nanorobots that will swim through and clean out your arteries," says Empedocles. "It's real, valuable technology that you will have in your hands in the next three to five years."

For his part, Empedocles is leading an effort at Nanosys to market efficient and supercheap nano-based solar cells that can go almost anywhere. The materials are made by mixing electrically conducting polymers with inorganic semiconductor crystals 10 to 60 nanometers in size. The materials convert solar energy to electricity with an efficiency approaching that of today's silicon-based solar cells but at one-tenth the manufacturing cost. Moreover, the nano solar cells could be embedded in roofing tiles—or even exterior paint—to provide electricity for homes, office buildings, and public transportation systems. Nanosys is joining forces with Matsushita Electric Works, a large Japanese manufacturer of building materials, to make the product. Look for nano solar cells in roofing tiles to be on the market by the end of 2006, says Empedocles.

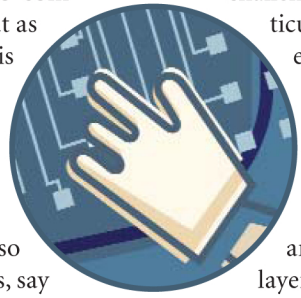
Nanosys has plenty of competition to get the first major nanotech products out the door, however. Two years ago, engineer **Colin Bulthaup** cofounded Kovio, now located in Sunnyvale, CA, to commercialize printable electronics based

...and more

BY GREGORY T. HUANG » ILLUSTRATION BY CELIA JOHNSON



on a nanofabrication process he developed as an MIT graduate student. The technique uses special inks made of metal or semiconductor particles just one to five nanometers in size, coated with a layer of organic molecules and dissolved in a solvent. The ink is stamped onto a plastic substrate and heated to expose the particles, which melt into patterns that produce integrated circuits. Because each layer of the new chips can be made in one step, without etching or photolithography, manufacturing time and cost could be one-tenth those of conventional silicon circuits. "We're not necessarily trying to compete with Intel, but we want to get as close to that as possible," says Bulthaup. The initial goal, he says, is to break into the market within three years with cheap, lightweight, and rugged electronics that will form the processing backbones of laptop displays, radio frequency identification tags, and personal digital assistants.



The first wave of nanotech products will also influence biotechnology within the next few years, say TR100 members. Building on his graduate research at Cornell University, **Stephen Turner**, cofounder and chief scientific officer of Ithaca, NY-based Nanofluidics, is developing a nanotech device that traps and directly analyzes individual strands of DNA. The technique will allow researchers to do gene sequencing at least a thousand times faster than they can using conventional methods that require large samples and painstaking preparation. And that could mean faster and cheaper blood analysis and contaminant screening. "Nanostructures are really an enabling technology for biotech," says Turner. He predicts that biochips sensitive and accurate enough for a number of commercial applications, including blood testing, could be available within five years.

Beyond the race to commercialize nanotech's first products, TR100 researchers are also laying the foundation for fundamentally new kinds of devices. **Peidong Yang**, an assistant professor of chemistry at the University of California, Berkeley, is building semiconductor nanowires that could eventually lead to advances in ultrahigh-speed optical communications, superfast processing, and ultradense data storage in computer chips. Yang is also developing nano-based thermoelectric materials that could be used to cool specific regions of chips, an application that becomes increasingly important as integrated circuits shrink in size. Indeed, the kinds of materials Yang is working on—fabricated on the nanoscale and, ideally, able to assemble themselves with little human intervention—could eventually transform the semiconductor industry by enabling the widespread manufacture of superhigh-performance electronics.

But that will take a while, and no one underplays the challenges in commercializing nano-based products, particularly in consumer electronics. "In a laboratory, it's easy to demonstrate a very good transistor. But when you go to large-scale manufacturing, there are a lot of challenges," says **Zhenan Bao**, a materials scientist at Lucent Technologies' Bell Labs. Bao is developing new kinds of organic semiconductors to make cheap, flexible displays and sensors. Common problems, she says, include layering different materials such that depositing one layer does not degrade the layers beneath it; getting molecules to organize into useful, reliable, and reproducible patterns; and connecting these structures to the macroscopic world.

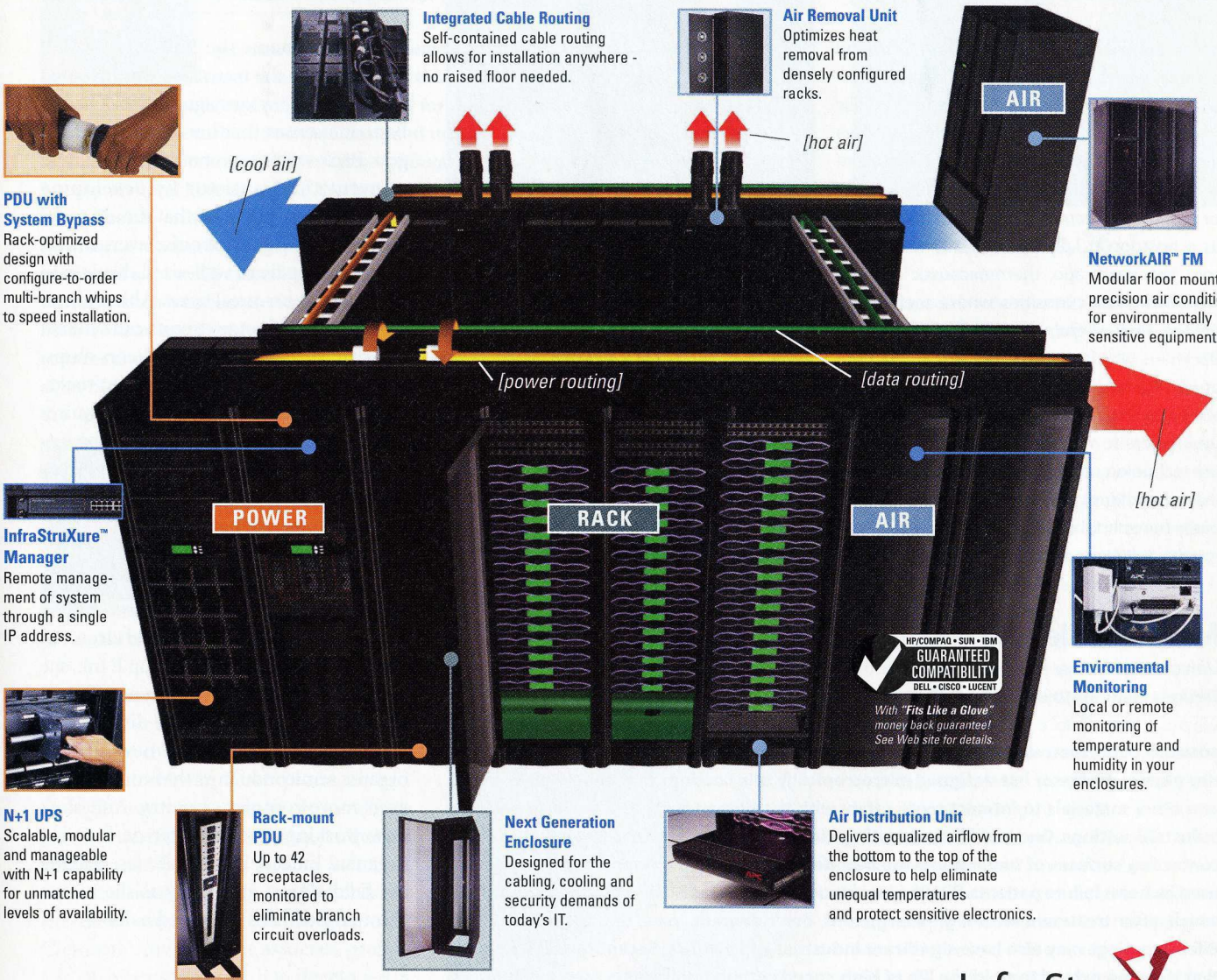
In the long run, the interfacing problem may be nanotech's greatest technical challenge. "You have to do more than get transistors to lay out," says physicist **Jordan Katine**, who is developing nano-based magnetic materials for computer memory systems at Hitachi Global Storage Technologies in San Jose, CA. "You need to address them, connect them in a controlled way, and get information in and out."

Amidst the confusion surrounding nanotech, however, the TR100 honorees say one thing is clear: this is a crucial time for the fledgling nanotech business. "This industry is going to be built on whether a few companies are able to deliver real technology," says Empedocles. It is also likely that the leaders of these companies—many of whom you'll meet in the next few pages—will become the new industry experts. And what they accomplish in the next several years could determine the future of not only nanotech and materials science, but also energy, computing, transportation, and biotech.

TR100 Startups in Nanotech, Materials, and Energy

INNOVATOR	COMPANY FOUNDED/COFOUNDED	STRATEGY/MILESTONES
Colin Bulthaup	Kovio (Sunnyvale, CA)	Nano-based particles and fabrication of cheap, printable, inorganic electronics for displays, radio frequency ID tags, and computers; has raised $19 million in venture capital
Stephen Empedocles	Nanosys (Palo Alto, CA)	Nanocrystal-based materials to make cheap, efficient solar cells, electronics, and sensors; has raised $55 million in venture investments
Cary Gunn	Luxtera (Carlsbad, CA)	Tiny optical-transmitting chips for ultrahigh-speed, low-power communications and processing; has raised $24 million in capital
Ravikanth Pappu	ThingMagic (Cambridge, MA)	Radio frequency ID tag readers and data security systems for logistics and inventory tracking; "agile reader" that works in all major frequency bands and interprets most radio frequency protocols
Manfred Stefener	SFC Smart Fuel Cell (Munich, Germany)	Micro fuel cells that use methanol to power laptops, traffic signals, and security systems; has raised 12 million euros from venture capitalists and other sources
Stephen Turner	Nanofluidics (Ithaca, NY)	Nano-based structures to do single-molecule DNA analysis, gene sequencing, and contaminant screening

If they come, you will build it.



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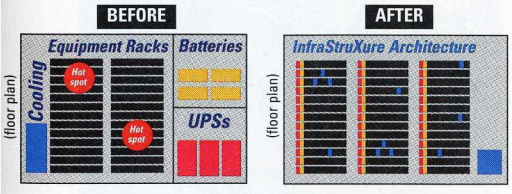

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Scott Backhaus, 35

Los Alamos National Laboratory

Invented a novel, high-efficiency engine powered by sound waves

SCOTT BACKHAUS is making waves—powerful acoustic waves that could cut the cost of industrial refrigeration. His tool is a thermoacoustic engine—a helium-filled pipe up to two meters long and 1.5 meters in diameter—that converts heat into sound waves, powering a chiller or producing electricity. When Backhaus began as a postdoc at Los Alamos National Laboratory five years ago, thermoacoustic engines were mere lab curiosities whose inefficiency limited their usefulness. Within five months, Backhaus, who is now a technical staff member at Los Alamos, engineered a feedback loop in the pipes that produced 50 percent more power from the same amount of heat. The resulting waves were so strong they wrecked his prototype, but the efficiency boost had suddenly made the technology practical. This spring, industrial-gases firm Praxair tested a thermoacoustic chiller using Backhaus's approach and intends to sell it for use in converting natural gas into a more easily transportable liquid form. The National Institute of Standards and Technology is also funding the development of Backhaus's acoustic engines for use in natural-gas power plants.

Marcela Bilek, 35

University of Sydney

Designs coatings to improve implanted medical devices and industrial tools

SOMEDAY SOON, Marcela Bilek's work may be dear to people's hearts. The University of Sydney physics professor has designed microscopically thin coatings that enable glass, metal, and other materials to interact more safely with the human body and perform better in industrial settings. One low-friction coating, currently in animal trials, protects the blood-contacting surfaces of implantable medical devices, such as the temporary heart pumps used by heart failure patients. Bilek's biocompatible coating seals the surface of the pumps, which, after treatment with high-energy ions, don't degrade, peel, or impair blood flow. Bilek's coatings may also have significant industrial applications. Recent tests have shown that they can extend tenfold the life of high-speed cutting implements used by automakers. Having earned an MBA from the Rochester Institute of Technology, Bilek feels comfortable predicting that her coatings could save manufacturers millions of dollars in tool replacement costs. She is also studying how her coatings might improve diagnostic instruments used in medicine.

Zhenan Bao, 32

Lucent Technologies' Bell Labs

Fabricates organic semiconductors used in flexible and cheap electronic devices

WALKING THROUGH the hallways of Bell Labs—where the transistor was invented more than 55 years ago—with Zhenan Bao, one senses that her brain is in high gear. Bao's ambition is nothing less than to reinvent the transistor by developing organic semiconductors that should make it possible to put electronics everywhere, in everything from wall-sized displays to price stickers on cereal boxes. Although organic semiconductor circuits can't match the computing power of silicon chips, they are potentially far cheaper to make. Producing silicon chips typically requires multibillion-dollar fabrication plants, but a modified ink-jet or silk-screen printer can pattern dissolved organic semiconductors on a pliable sheet of plastic.

Bao crafted a plastic all-printed circuit in 1997. Collaborating with startup E Ink, she then helped create a prototype of electronic paper, a thin, flexible display. Bao subsequently discovered a new class of organic semiconductors that could enable even more complex circuitry. And she's now working on still better-performing organics. Indeed, Bao's efforts are driving the field almost as quickly as she moves through Bell Labs' hallowed halls.

Daniel Bond, 34

University of Massachusetts

Turns sea muck into fuel cell power plants

TURNING THE muck at the bottom of the ocean into a valuable source of energy is a lot less improbable than it might seem, thanks to microbiologist Daniel Bond. Three years ago U.S. Navy researchers discovered that a graphite rod stuck in sea muck generates microwatts of electricity. This past year Bond helped explain why. The senior research fellow at the University of Massachusetts showed that bacteria collect on the rod, feed on organic compounds in the muck, and transfer electrons to the graphite, creating a current. Bond and colleagues have since turned that insight into a practical fuel cell. Bond places the bacteria inside a glass chamber and feeds them organic matter; in response, the bacteria create a usable current. The bacteria in the fuel cell can feed on contaminants such as toluene. Bond's goal is to optimize the fuel cells to generate large amounts of electricity. If he succeeds, the bacteria-based fuel cells could transform sewage plants into power plants.

Michael Bowman, 31

General Electric

Builds microturbines that could become the power plant of choice in many settings

MICHAEL BOWMAN is producing prototype turbines just 1.5 meters tall and two meters long that could provide everything from backup power in office buildings to primary power for remote areas of developing countries. The natural-gas microturbine Bowman designed uses a proprietary combustion chamber and electronics to produce 175 kilowatts—enough to supply a small hospital, or about 20 houses. General Electric claims the turbine is more efficient and less polluting than anything already on the market and estimates that it will be commercially available in 2006. Bowman, a mechanical engineer and manager of GE's energy systems laboratory, says, "We leveraged a lot of GE technology on larger machines to develop a low-cost solution." And that approach is consistent with his career ambitions: to adapt specialized technologies for massive markets. Bowman's previous GE designs include a motorized turbocharger that reduces engine startup emissions in diesel locomotives and trucks. His sights are now on an even bigger prize: making hydrogen power practical. Bowman leads 10 researchers who are exploring ways to use wind and geothermal systems to drive electrolysis, which extracts hydrogen from water. "We have a very novel idea in the process of patenting," he says, which he hopes could help wean the world off fossil fuels.

Karen Burg, 35

Clemson University

Engineered a minimally invasive process to rebuild tissue for breast cancer survivors

KAREN BURG wants to heal the minds and bodies of women who survive breast cancer. The psychological and physical trauma of lumpectomies and mastectomies is bad enough, but many women also undergo reconstructive breast surgery, enduring general anesthesia and risking infection from incisions, implants, and stitches. At the tissue-engineering lab Burg runs at Clemson University, the associate professor of bioengineering has developed a minimally invasive process for rebuilding breast tissue. Burg has designed tiny, degradable synthetic beads on which a patients' own fat cells can be cultivated. A degradable gel is added to help temporarily bind the beads and cells, which are injected into the damaged tissue. In laboratory tests, injected cells reproduced and meshed with native cells, and the beads decomposed as the new tissue grew to support itself. Burg hopes to begin human trials of the method soon; the National Institutes of Health may provide an infusion of nearly $3 million for the effort. Burg is also assessing ways to apply her tissue-engineering techniques to the repair of ruptured spinal discs.

Xiangfeng Duan, 26

Nanosys

Transforms nanowires into incredibly small transistors for powerful, flexible computers

FIVE YEARS after moving from China to Massachusetts, Xiangfeng Duan had earned a PhD from Harvard University in physical chemistry and moved to the forefront of nanotechnology research. Last year he joined Palo Alto, CA-based startup Nanosys as a staff scientist to help create practical technology using semiconducting nanowires. Duan and his colleagues developed a method for fabricating nanowires two to 100 nanometers in diameter and up to hundreds of micrometers long. They also devised techniques for organizing these nanowires into functional electric circuits. Using these techniques, Duan has built transistors 10 times smaller than conventional ones and has made tiny light-emitting diodes. He has also shown how nanowire arrays can be mounted on flexible substrates, which could lead to foldable or wearable computers. Investors have poured more than $55 million into Nanosys since its founding in 2001, and roughly half the company's efforts are based on Duan's research. So the startup's investors can't wait to see what Duan will accomplish next using his nanotech bag of tricks.

Colin Bulthaup, 26

Kovio

Developed new fabrication methods that could slash the cost of chip manufacturing

THERE HAS to be a cheaper way to make computer chips, and Colin Bulthaup thinks he has found it. Current manufacturing involves multibillion-dollar fabrication plants that use time-consuming photolithography methods to painstakingly etch features onto semiconductor microchips. But as an MIT grad student, Bulthaup developed a method that uses a liquid embossing system to directly print patterns of inorganic semiconductors on the chips. And because the technique—which requires no etching—can cheaply deposit multiple layers of complex circuits, even on flexible substrates, it can be used for such applications as inexpensive electronic tags. After earning a graduate degree, Bulthaup and three partners initially raised $7 million to start Sunnyvale, CA-based Kovio, which is aiming to commercialize the technology. Bulthaup predicts his approach will cut the cost of chip manufacture by a factor of 10 and says that electronic devices made with the printing technology will be available in 2005.

Stephen Empedocles, 34

Nanosys

Formulates business strategy for one of nanotech's leading startups

STEPHEN EMPEDOCLES wasn't looking for a career in business development. But in helping transform nanotechnology from a largely academic exercise into a fledgling industry, he found one. After earning a PhD in physical chemistry from MIT and joining Quantum Dot of Hayward, CA, an early nanotech startup, Empedocles realized

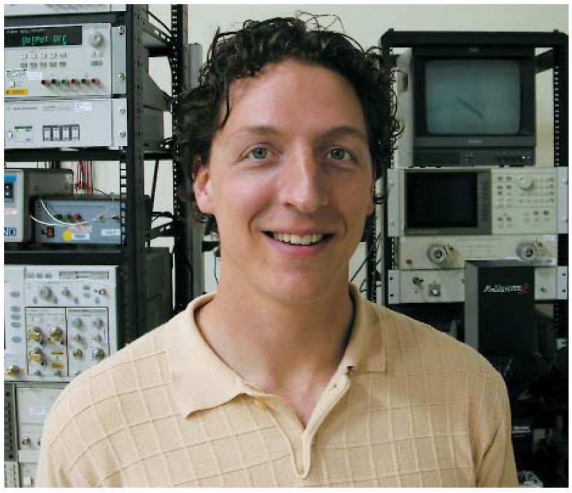
there was a critical lack of people with both business and technical expertise in the nanotech world. The consequence was a gap between scientific realities and market expectations, and Empedocles stepped in to develop the business strategies to bridge the gap. He helped devise novel ways to use nanocrystals for biological testing and played an important role in finding Quantum Dot more than $37 million in venture financing. In 2001 he left Quantum Dot and cofounded Nanosys in Palo Alto, CA. The company's goal, says Empedocles, director of business development, is to commercialize nanotech's first blockbuster products within three years. Combining his technical insight and business savvy, Empedocles has identified several candidates, such as building materials impregnated with nano solar cells. Recently, Nanosys signed a deal with Matsushita Electric Works to develop the nano solar-cell technology. Overall, Nanosys has raised $55 million in investments. If Empedocles can pull off that first big product, his transformation from scientist to entrepreneur will be complete.

Cary Gunn, 30

Luxtera

Shrinks optical circuitry to speed transmissions on phone and Internet networks

CARY GUNN is changing photonics—the use of laser light for computing and telecommunications. A long-term goal of the field is to etch optical circuitry onto silicon wafers so it can manipulate light the way electronic circuitry manipulates electrons. To make the technology widely useful and cost effective in telecommunications networks, engineers have been trying to decrease the size of optical components and integrate them with electronics on individual chips. When Gunn was a Caltech graduate student, he used proprietary computer simulation tools to design fine-scale optics that enabled tiny optical components—one-hundredth the size of conventional ones—that operate with unprecedented precision. The improvement makes it practical to integrate optical and electronic components. Such integrated microprocessors could communicate with the outside world at much higher data rates than separate chips can manage, while using less power. To develop the technology, Gunn and five associates raised $24 million from venture capitalists and started Luxtera in Carlsbad, CA. Gunn, who is vice president, says Luxtera should have integrated chips on the market by next year.



Vladislav Gavrilets, 28

Athena Technologies

Designs flight control technology that could lead to unmanned, autonomous helicopters

FOR VLADISLAV Gavrilets, mathematics has wings. As a PhD candidate at MIT, he built an avionics system that enabled a one-and-a-half-meter-long, unmanned helicopter to complete programmed flips and rolls without human intervention. The two-time junior chess champion of Kyrgyzstan studied an expert pilot's strategy for performing aerial maneuvers, modeled it mathematically, and created algorithms to execute it. Then he wired up an onboard, custom flight control box containing sensors, including a Global Positioning System receiver and an altimeter to monitor the helicopter's position, and a radio that transmitted data to a ground-based processor. Fed with such real-time information, the processor continuously updated flight instructions. Recently, Gavrilets used his algorithms to demonstrate how the helicopter can complete an air show routine. He hopes improved processing will lead to unmanned helicopters that react to unexpected obstacles. Eventually, such helicopters could perform military reconnaissance or film aerial scenes for movies. Gavrilets is now a manager of control systems development at Athena Technologies in Warrenton, VA, which makes miniature autopilots for unmanned aircraft.

Scott Gaynor, 32

Dow Chemical

Devises processes used to make polymers with improved properties

FOR SCOTT Gaynor, hunting for new polymers in the lab is "just like the hunting I did as a boy: you never know what's behind the next tree." As assistant director of the Macromolecular Engineering Laboratory at Carnegie Mellon University, Gaynor discovered catalysts that led to a new technique for synthesizing versatile and customizable polymers. Gaynor then played a lead role in developing the process to make polymers that could be used in everything from coatings to microelectronics to cosmetics. The technology is now being investigated by dozens of manufacturers worldwide for use in commercial applications. The process, "atom transfer radical polymerization," is more tolerant of water, dust, and other impurities than other polymerization processes, a plus in industrial settings. Gaynor, who holds 10 patents and has three more pending, joined Dow Chemical in 2000, where he has developed new techniques to synthesize variants of common plastics, with improved properties. Gaynor is now preparing light-emitting polymers that could result in video displays that are thinner, sharper, and brighter than current flat-panel liquid-crystal displays.

Yu Huang, 27

MIT

Fashions three-dimensional grids of nanowires that act as electronic circuits

CHINESE-BORN Yu Huang came to the United States in 1999 to pursue an advanced education in materials science. It didn't take long, however, before she developed creative new ways to make nanoelectronics. One of her first breakthroughs was a method for controlling the assembly of circuitry made from semiconducting wires less than 100 nanometers in diameter. Huang, who received her PhD in June from Harvard University and is now a Lawrence Livermore fellow at MIT, suspended

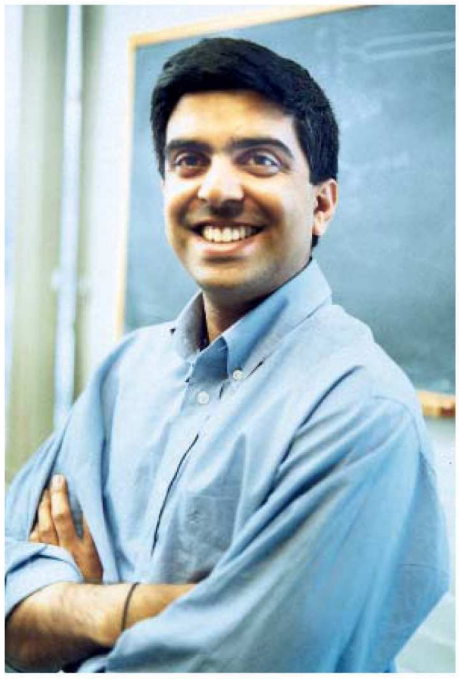
nanowires made of silicon and other materials in an ethanol solution. She then forced the fluid through tiny channels in a plastic mold, creating parallel nanowire arrays. Using the method, she built nanowire grids that could function as electronic circuits. She also demonstrated that she could build up layers of arrays, creating three-dimensional circuitry. Huang says her approach, unlike other methods of assembling nanowires, could be scaled up to produce millions of devices at a time. Even though practical products are likely at least a decade away, several computer chip manufacturers, including Intel, have expressed interest.

David M. Lynn, 30

University of Wisconsin-Madison

Synthesizes polymers that are better able to deliver therapeutic genes

WHEN DAVID Lynn was doing graduate work in chemistry at Caltech, he became fascinated with polymers and their possible biomedical uses. One such possibility is that polymers could deliver therapeutic DNA to cells to treat conditions such as cancer or cystic fibrosis. Other researchers pursuing gene therapy have used modified viruses to carry genetic material into cells, but viruses can provoke serious immune reactions. The right polymer could make a much safer delivery agent, because the immune system is far less likely to perceive it as a threat. As a postdoc at MIT, Lynn developed a process that could synthesize hundreds—or even thousands—of new polymers at once and screen their varying DNA-transferring capabilities. His approach has already identified several new polymers that excel at gene delivery. Now an assistant professor of chemical and biological engineering at the University of Wisconsin-Madison. Lynn has two patents issued or pending relating to his process and has been approached by several companies.



Krishna Kumar, 32

Tufts University

Improves the stability and effectiveness of protein-based drugs

PROTEINS ARE marvels of nature, but because they can be fragile and unstable, many protein-based drugs break down and lose effectiveness. Krishna Kumar, an associate professor of chemistry, heads a Tufts University research team that is engineering better proteins. In one approach, Kumar and his associates chemically alter segments of the proteins, stiffening their structures and improving their stability. In a process that incorporates fluorocarbons like those found in Teflon, the team fabricates proteins that can penetrate human cells, opening portals through the cell membranes to allow the passage of drug molecules. Kumar's team has received one international patent, and other patents are pending. Several biotechnology and pharmaceutical companies, as well as venture capital firms, are evaluating Kumar's techniques for their potential to make drugs more effective. If they work, then the flood of new information about the proteins in the human body could soon yield better therapeutics.

Jordan Katine, 34

Hitachi Global Storage Technologies

Makes higher-density hard drives using magnetic nanomaterials

ALTHOUGH PRACTICAL nanotechnology devices are often portrayed as being years away, Jordan Katine is making them part of the present. In 1999, Katine demonstrated how to alter a nanomaterial's magnetic orientation by sending a "spin-polarized" current through it—a current composed of electrons all spinning in the same direction, rather than in random directions as in common electrical current. To exploit this effect and boost the density of magnetic storage, Katine made "nanopillars" smaller than 100 nanometers across, composed of a magnetic layer at each end separated by a copper layer. By sending spin-polarized current through the pillar, he got its electrons to spin in the same direction and aligned the magnetic layers; reversing the direction of current flow reversed the electron spin, which flipped the magnetic layers back. The nanopillars can assume one of two magnetic states, and thus can serve as bits in storage systems. Katine, a research staff member at Hitachi Global Storage Technologies in San Jose, CA, has already used a similar technique to pack more bits onto magnetic recording heads in computer hard drives that Hitachi is selling. Much as the former College Bowl whiz enjoys publishing in *Physical Review Letters*, he also likes going to Circuit City and saying, "I built this."

KATHLEEN DOOHER (KUMAR)

David A. Muller, 35

Cornell University

Images the individual atoms that are critical to a transistor's electronic properties

MICROSCOPY MAESTRO David A. Muller knows that many of the features of silicon transistors in computer chips will soon shrink down to the nanoscale. That makes the South African native's imaging research crucial to the transistor's future. The electronics industry inserts "dopants," or impurities, into silicon to control its electrical properties. In the smallest transistors, only one or two dopant atoms could determine the success of a device, which makes it essential that manufacturers understand how dopants function on the nanoscale. Muller has used an electron microscope to directly observe individual dopant atoms of antimony, measuring their structural arrangement, electrical properties, and other traits. Muller, an associate professor of applied and engineering physics at Cornell University, compares the task to locating a few pins in a haystack the size of the United States.

Balaji Narasimhan, 32

Iowa State University

Devises time-release polymers to replace multiple vaccine injections

CHEMICAL ENGINEER Balaji Narasimhan is determined to help prevent common worldwide diseases such as tetanus and diphtheria. These illnesses currently require four to five injections to build up a subject's immunity, a fact that is particularly troublesome in populations with limited access to health care. Narasimhan, an associate professor at Iowa State University, is trying to achieve the same effects with a single dose, by encapsulating vaccines in specially tailored biodegradable polymers. When injected, the polymers slowly release the vaccines in precise amounts at precise times over a one-year period, thereby maximizing immune response and making booster shots unnecessary. The precision that Narasimhan has achieved in lab tests is better than that for previous drug encapsulation systems. Narasimhan is also devising noninteractive polymers to deliver fragile proteins involved in cancer therapies. One advantage is that his polymers resist water, and thus degradation, better than other drug delivery materials. Narasimhan expects both systems to be ready for human testing within five years. Before his work with polymer-based drug delivery, Narasimhan and researchers from the Swiss chemical company Clariant invented a more efficient process for making photoresists—polymers used in the manufacture of computer chips. Clariant is now operating a pilot photoresist production facility in New Jersey that uses this process.

Yasunobu Nakamura, 35

NEC Fundamental Research Laboratories

Achieved a breakthrough that could help make quantum computing a reality

WHILE EXPERIMENTING with ultrasmall superconducting transistors at NEC in Tsukuba, Japan, Yasunobu Nakamura became familiar with quantum computing and had a vision. Each of his transistors featured an island of aluminum just 20 nanometers thick—so small that its state could be altered with a single electron. This exquisite sensitivity was exactly what was needed to create a quantum bit, or qubit, the fundamental element of quantum computing, which promises some day to speed computation exponentially. One of quantum computing's basic requirements—which had been contemplated for two decades—was controlled operation of a qubit, and Nakamura achieved it in 1999. By applying voltage pulses of varying lengths, he dictated whether the island had an extra pair of electrons (the *1* state), no extra electrons (the *0* state), or a combination of the two—a quantum-mechanical state that enables qubits to store far more information than conventional bits. Next, Nakamura and a collaborator got two qubits to interact in a manner that had been predicted but never demonstrated. The challenge ahead is to control coupled qubits long enough—microseconds—to perform meaningful computations. Meanwhile, Nakamura says, people should start preparing some good applications for quantum computers.

Ravikanth Pappu, 34

ThingMagic

Fights credit card forgery with glass-bead "keys"

WHEN A credit card company asked the MIT Media Lab to develop a technique to produce card identifiers that, unlike magnetic stripes, would be extremely difficult to forge, graduate student Ravikanth Pappu devised a cheap and simple solution. He embeds hundreds of glass beads into dime-size epoxy tokens. When a laser shines on a token, its beads scatter the light in a unique pattern that can be digitally stored as a fingerprint or "key." Retailers could use readers to check patterns against keys in a secure database. Pappu says there is no known technology that can counterfeit the tokens or their keys. Now a principal at ThingMagic in Cambridge, MA, which is developing "embedded intelligence" as well as radio-frequency identification technologies, Pappu says credit card companies are calling, interested in building tokens into their cards. The technique could also be used for tamper-resistant packaging, or to create identifiers for computer chips. According to Neil Gershenfeld, Pappu's MIT advisor, cryptographers are often very critical of new ideas, but they have "welcomed this new approach."

atomic Digital Technology

Never set your watch again!

Atomic digital watches keep absolute time and date accuracy by tuning in to the official time transmitter.

The world has become a smaller place in the past few decades. Transactions take place across the world in an instant. Having a timepiece that can not only keep perfectly accurate time, but also keep track of the time zones can be really helpful and convenient. Now there is a watch that scientifically gives the right time in all zones within a 2,000 mile range of the F-1 Fountain Atomic Clock.

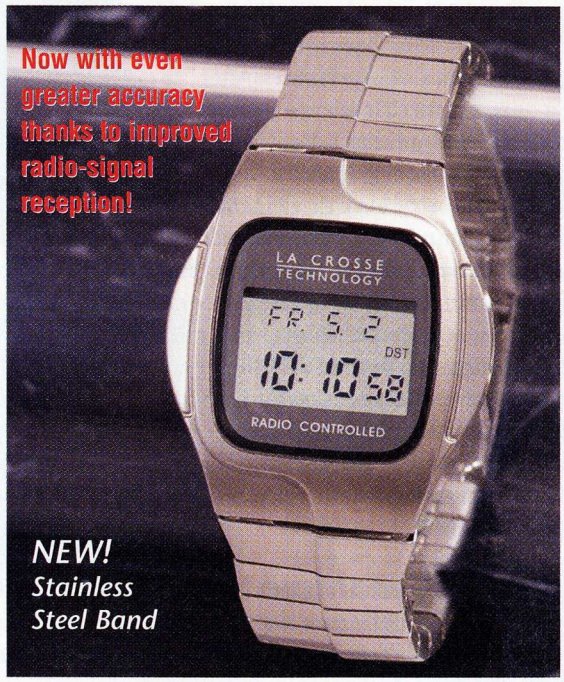
If you travel this watch is a necessity. The Atomic Digital Watch from LaCrosse Technology is radio-controlled, maintaining its incredible accuracy by automatically tuning into the official standard frequency and time transmitter in North America. This WWVB radio signal gets its time from the most precise clock in North America based in Colorado, and transmits its signal over a 2000-mile range. With the press of a button, the Atomic Digital Watch gives you a selection of 24 time zones, from GMT+12h to GMT-12h with special U.S. time zones displayed with three characters (ATL, EST, CST, MST, PST, ALA, and HAW). This ultra-accurate radio-controlled timepiece has a perpetual day and date calendar, signal reception indicator and is powered by a 3-volt lithium battery expected to last up to three years.

Radio wave technology

Does anyone really know what time it is? Well, the U.S. Government wants to, so they created the National Institute of Standards and Technology, a component of the U.S. Department of Commerce. The Time and Frequency Division, located in Boulder, Colorado, maintains the F-1 Fountain Atomic Clock, the nation's standard of time. This clock neither gains nor loses a second over a 1 million-year period. This clock is used to create an international time scale, which NIST distributes through its radio stations.

Wrist-worthy. Now, advanced Radio Frequency (RF) technology is featured in a wrist-worn timepiece for use at home, at the office or on the road. This watch is the next best thing to having your own atomic clock, because it automatically displays the precise accurate time thanks to its improved radio-signal reception. With a 12 or 24-hour time mode capability, it automatically adjusts itself for daylight saving time (with an "OFF" feature) and leap years and it features a variety of practical and convenient features to fit your lifestyle.

A timely gift. The stainless steel butterfly clasp and removable links to adjust the band size make it a good fit.



The specially designed casing allows for optimal radio-signal reception. This watch is a great gift for anyone who values precision and technology.

Try it for yourself. Advances in electronic technology let you get precise timekeeping at an affordable price. Now, thanks to a factory-direct relationship with the manufacturer of the Atomic Digital Watch, you can try it for yourself with TechnoScout's exclusive home trial. Try this product for 30 days and return it for the full purchase price if not satisfied.

Atomic Digital Watch-*Stainless Steel Band*

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Ainissa G. Ramirez, 34

Yale University

Formulated an advanced universal solder for electronics and optics

AINISSA RAMIREZ discovered a long-sought prize of metallurgy: a universal solder that can bond metals to ceramics, glass, diamonds, and, notably, the oxide materials used in semiconductor fabrication. Researchers had been hunting for such a compound for decades: the limitations of available solders have often meant electronic- and optical-device failures. After earning a PhD in materials science at Stanford University and joining Lucent Technologies' Bell Labs in 1998, Ramirez found that mixing certain rare-earth elements, particularly lutetium, into solder metals vastly improved their bonding capabilities. Her solder is the first that can join all kinds of inorganic materials with high-strength bonds, and has the potential for extensive use in the electronics, optoelectronics, and microelectromechanical-systems (MEMS) industries. Ramirez also devised thin-film coatings that lessen damage caused to MEMS components by thermal expansion during operation, and she fabricated alloys that were key to Bell Labs' making a high-speed all-optical switch. Now an assistant professor of mechanical engineering at Yale University, Ramirez finds it odd that metals are "often overlooked" as a field for innovation. "These materials are fundamental," she points out.

Christian Rehtanz, 35

ABB

Adds smarts to high-voltage power lines so they can deliver more electricity

ELECTRIC-POWER grids are often categorized as the world's largest machines, but they are not the most sophisticated. Grid operators have little data on how weather, shifting electricity consumption, and other factors affect power flows minute to minute over the grids' high-voltage main lines. So to be safe, utilities cap the power a line carries at well below its physical limits—a drawback, given rising electricity demands. To increase capacity, grids need more smarts, and that's what Christian Rehtanz gave them, at Zürich, Switzerland-based ABB. Rehtanz devised algorithms that use information from sensors distributed around the grid to monitor a power line—or several lines in a transmission corridor—and calculate in real time how much power it can safely carry. He then led a team that turned these algorithms into a commercial monitoring, protection, and control system for utilities, dubbed PSGuard.

Norwegian utility Statnet is already testing Rehtanz's hardware and software on a massive high-voltage corridor to Sweden, and Rehtanz predicts Statnet will be pushing 10 percent more megawatts by year's end—potentially enough to supply electricity to an additional 100,000 homes. Rehtanz has since powered up, too; he now leads technology development for ABB's 8,000-person global power systems business.

Manfred Stefener, 33

SFC Smart Fuel Cell

Constructs small fuel cells to efficiently power laptop computers

LAPTOP-COMPUTER users are still slaves to batteries that fade after a few hours. Manfred Stefener, managing director and founder of SFC Smart Fuel Cell in Munich, is leading the way to an alternative: small fuel cartridges that use methanol to generate electricity, emitting only water vapor, carbon dioxide, and heat. Stefener's company and German laptop maker Medion have partnered to develop and commercialize an energy docking station, which will provide up to 10 hours of power before needing a new fuel cartridge. While it will add some bulk—the product will be docked under the laptop—"They are delivering where other companies have not," says Robert Hockaday, founder of Energy Related Devices, which is also developing micro fuel cells. Stefener, a chemical engineer, is working on business questions too, such as how customers can easily obtain replacement cartridges. The company is also commercializing its fuel cell system to power other applications, such as traffic signals. And Stefener says the company is working on a fuel cell that can be integrated right into the laptop, avoiding the bulky docking station.

Claire Tomlin, 34

Stanford University

Writes software that could alleviate air congestion and lead to far fewer delays at airports

FORGET ABOUT the need to build more runways; Claire Tomlin's computer models and software could eliminate airport congestion. The assistant professor of aeronautics and astronautics at Stanford University has created prototype software that allows planes to detect one another, fly closer together, avoid bad weather, and automatically maneuver to avoid midair collisions. Using the system, air traffic controllers might achieve far greater efficiencies, which should translate into fewer delays for passengers. Although testing for commercial air traffic use is still a decade away, Boeing researchers in St. Louis, MO, already use Tomlin's software to ensure safe coordination of groups of unmanned aerial vehicles. Tomlin's innovations make her a leader in a new field that provides both optimal solutions to complex logistical problems and ultrasafe software control of mechanical systems, says Richard Murray, a mechanical engineer at Caltech. Tomlin's methods, he says, are critical for anyone who "cares about verifying that systems do what they are supposed to do." Her advanced software won't be ready for use in civilian aircraft for at least 10 years, but because of her work, change is already in the air.

Stephen Turner, 35

Nanofluidics

Built a tiny device that greatly speeds up DNA sequencing

STEPHEN TURNER admits he's a compulsive inventor: "Whenever I see a device, I think about how to make it better." At 12, Turner used wires, batteries, and wood to make a light switch his parakeet could operate. As a Cornell University postdoc, he built a minuscule gadget that significantly speeds up the sequencing of DNA. The nano device is just big enough to hold one DNA molecule, one polymerase molecule, and assorted nucleotides. The polymerase copies the DNA using fluorescently labeled bases as building blocks. An optical detector reads the bases, one at a time, as they are assembled. Turner says the approach is more cost effective than standard sequencing methods because it requires fewer DNA strands and reagents, and it is potentially 1,000 times faster. Moreover, a million of these nano devices could fit on a chip the size of a penny, supporting a million reactions simultaneously. Turner predicts that the technology could sequence the entire genome of an individual in hours, which would bring much closer the idea of genetic-based personalized medicine. Turner is now chief scientific officer at Nanofluidics, a Cornell spinoff in Ithaca, NY, where he plans to commercialize the technology within five years.

Ralf Wehrspohn, 33

University of Paderborn

Fabricates nanotube crystals that can route optical telecommunications signals faster than competing chips

THE UNIVERSITY of Paderborn's Ralf Wehrspohn is one of Germany's youngest physics professors and an expert in manipulating light. One key to future optical devices could be crystals made from materials such as silicon or aluminum oxide. Four years ago, at the Max Planck Institute, Wehrspohn constructed and patented a stamp-like tool embossed with billions of microscopic pyramids that impose a grid of tiny perforations on the materials. He and his colleagues then used acids to burrow into the perforations, creating a perfect array of holes. They melted a metal or polymer over the template, forming nanotubes of specific depths and widths in the holes. Light passing through the resulting nanoarray can be "steered" by electrical fields. Wehrspohn is now collaborating with Infineon Technologies to develop an all-optical chip that reroutes communications signals faster than current routers. He is also working on a compact sensor that measures how light flow is altered by alcohol in a person's breath.

S. Travis Waller, 29

University of Texas at Austin

Writes algorithms that determine why traffic jams form and how to ease them

WHEN S. Travis Waller, a native of tiny Ironton, OH, first experienced the traffic snarls of Chicago, he was shocked. Clearing congestion is now his work. The fundamental research tool in his field is software that models traffic flow, but until recently, the models were capable of representing only static traffic conditions. Waller wrote algorithms that allow for dynamic modeling of changing conditions. As a postdoc at Northwestern University, he led the development of modeling tools based on the algorithms and made them available on the Web. Waller and others are using these tools to analyze traffic-congested areas and specify the most effective long-term investments in infrastructure improvements. Now an assistant professor of civil engineering at the University of Texas at Austin, Waller is also devising an online routing system that uses onboard computers to tell drivers which routes offer the quickest paths given current traffic patterns. Hoping to identify the conditions that slow traffic, he is working with the city of Chicago to test the system by tracking transponder-equipped buses. Eventually, the system could feed data to a central controller that would change red lights to green to improve traffic flow.

Peidong Yang, 32

University of California, Berkeley

Assembles nanowires that could revolutionize lasers and computers

IF NANOELECTRONICS is ever to fulfill its promise of supplying vastly smaller and more powerful computers, researchers will need to invent the right materials. No one knows what those will be, but University of California, Berkeley, assistant chemistry professor Peidong Yang believes inorganic nanowires offer tantalizing possibilities. Such wires are only a few nanometers in diameter, but they can be several micrometers long; Yang says those dimensions make them "naturals" for integrating nanoelectronics with larger-scale devices. Using a light-emitting nanowire, Yang has built a tiny laser, an invention that could revolutionize ultradense data storage. He has also used a combination of semiconducting materials to form single nanowires that could act as tiny light-emitting diodes, and has made nanowires that show promise as highly efficient thermoelectric materials for converting heat into electricity. Still, Yang acknowledges that challenges remain before these creations yield commercial devices. Chief among them, he says, is finding ways to assemble millions of nanowires into a desired device. Yang is pursuing several research projects to achieve just that.

Where are they now?

IT GOES WITHOUT saying: once a TR100 winner, always a TR100 winner. So the last thing we'd do is lose sight of the 200 honorees we've previously recognized in the magazine and at our Young Innovators and TR100 conferences. We're keeping tabs, and the information we have should surprise nobody. Yes, even in the aftermath of the so-called dot-bomb, those remarkable, groundbreaking researchers and inventive entrepreneurs continue taking risks—forming companies, raising venture capital to expand existing enterprises, unveiling technological breakthroughs, and otherwise exploring new frontiers. BY BRAD STENGER

Launches

Daniel Branagan (2002) is now chief technical officer of NanoSteel in Maitland, FL, founded in 2002 to commercialize the superhard steel alloys he invented when he was working for the Idaho National Engineering and Environmental Laboratory in Idaho Falls, ID.

Last September, former Inktomi chief technology officer **Steve McCanne** (2002) founded NBT Technology in San Francisco with $6.6 million. Shifting focus from ideas McCanne pioneered at an earlier startup, FastForward Networks, NBT aims to eliminate wide-area network bottlenecks by using software that improves network application performance for customers with far-flung operations.

Professor **Adam Arkin** (1999) of the University of California, Berkeley, serves as director of the Virtual Institute for Microbial Stress and Survival, which he founded. Funded with a $36.6 million grant from the U.S. Department of Energy, the institute's first project—an investigation of various microbes and the ways they neutralize toxins—involves researchers from the Lawrence Berkeley, Sandia, and Oak Ridge National Laboratories, San Diego-based Diversa, the University of Washington, and the University of Missouri. Arkin believes the effort could uncover cost-effective ways of using microbes to clean hazardous-waste sites.

European Bioinformatics Institute researcher **Ewan Birney** (2002) posted Genome KnowledgeBase on the World Wide Web in February 2003. The site, at www.genomeknowledge.org, provides a forum in which collaborators worldwide can contribute their findings about the functioning of human genes.

Dan DiLorenzo (1999), a neurosurgeon and adjunct biomedical engineering professor at Tulane University, has formed NeuroBionics. The Boston startup is developing an implantable self-regulating device DiLorenzo invented to control electrical signals of the nervous system. He says such brain "pacemakers" might one day treat conditions including Parkinson's disease, epilepsy, obesity, and depression.

Last July, **Steve Tuecke** (2002) of Argonne National Laboratory in Illinois released the Globus Toolkit 3.0 for grid computing. Among its applications, grid computing plays a major role in the $10 billion On Demand business strategy IBM announced in October 2002. On Demand makes it possible for participating companies to tap into a vast network of computing power much the way they use electricity—by plugging in and paying as they go.

Capital Gains

The sensing and controlled-release technology **John Santini** (2002) is developing for drug delivery won't be ready for a few more years. However, the $16 million in venture capital he raised during 2002 should smooth the road to development for MicroChips, his Bedford, MA, company. Recent work has been encouraging. Santini reports that chip implants in animals performed well over a seven-week period, and three- to six-month-long tests have been scheduled.

During the first half of 2003, **Vivek Subramanian** (2002), a professor at the University of California, Berkeley, helped raise $67 million for Matrix Semiconductor, the company he founded in Santa Clara, CA. Subramanian says that within five years he hopes to have produced disposable plastic semiconductors that will store information and use radio frequency technology to communicate with mobile phones or handheld readers. He expects that the semiconductors will cost less than a penny apiece, making them more viable than conventional bar codes.

Last May **Helen Greiner** (1999), president of iRobot in Burlington, MA, secured a $13 million infusion that will help her company maintain its market position. The funding will support such products as iRobot's Roomba, a robot vacuum cleaner that sells for $200, and the $50,000 PackBot, a pug-size robot with a surveillance camera. The U.S. Army used PackBots to search buildings during the 2003 invasion of Iraq.

Armed with $25 million in venture funding raised late last year, **Carmichael Roberts** (1999), president of Surface Logix in Brighton, MA, used the company's core

chemistry and soft-lithography technologies to develop organic semiconductors that simulate a range of human biological responses to disease more accurately than animal models can. Roberts expects the precise architecture of these microenvironments to help pharmaceutical companies speed drugs to clinical trials.

Breakthroughs and Milestones

Last March, pilot tests of the PicoPeta Simputer, a handheld device developed by **Ramesh Hariharan** (2002), were completed in India. Village accountants with no computer experience successfully uploaded data about harvests to central servers that tabulated results and set crop prices. Hariharan's manufacturing partner, Bharat Electronics, aims to have the Simputer in stores by year-end.

Together with two colleagues, **Pamela Lipson** (2002), founder of Cambridge, MA-based Imagen, engineered what Guinness World Records declared the world's smallest reproduction of a book—a five-millimeter-by-five-millimeter edition of the New Testament written in 24-karat gold. Such minuscule printing could be used in identifiers on sensitive materials, foiling thieves and counterfeiters. Image-processing techniques Lipson and Imagen developed are currently being used by Boston-based Teradyne, a manufacturer of automatic inspection equipment, to test electronic components of cell phones, computers, and handheld game machines.

This past spring, **Sean Morrison** (2002), an assistant professor and researcher at the University of Michigan, discovered that the Bmi-1 gene plays a crucial role in the ability of stem cells found in adult tissues like bone marrow to "self-renew"—to divide in such a way that they give rise to more stem cells. Without Bmi-1, stem cells become depleted. If scientists can harness the regenerative power of stem cells, it may be possible to culture them in the laboratory and use them to treat Parkinson's disease and a wide variety of other ailments that develop as a consequence of cell death.

Stanford University's **Vijay Pande** (2002) accomplished a long-sought goal of computational biology: starting with genome sequence information, he simulated protein folding. Genes provide the recipes for building proteins—the strings of amino acids responsible for many vital functions in the body—but when proteins fold incorrectly, they can become toxic. Pande believes that the ability to correct such mistakes could lead to cures for such ailments as Alzheimer's disease, Cystic Fibrosis, and Creutzfeldt-Jakob, or mad-cow, disease.

Cryptographer **Vincent Rijmen** (2002) helped Cryptomathic in Brussels, Belgium, release its electronic-voting and digital-signature products. Encryption can be used to validate e-votes while preserving voter anonymity, supporting legitimate elections under the scrutiny of independent observers. A pilot e-voting test for the European Union is under way.

David Sabatini (2002) of the Whitehead Institute for Biomedical Research in Cambridge, MA, won a patent in April for his "reverse-transfection method" for assembling DNA microarrays. These computer-chip-sized devices are dotted with genes or other biological agents, which can be simultaneously tested against therapeutic compounds. Sabatini's reverse-transfection microarrays could help researchers and drug companies study thousands of interactions of proteins and prospective drugs in a single hour—up to a million per day. Akceli, the Medford, MA, startup Sabatini cofounded, licenses the technology exclusively.

Samir Mitragotri (1999), a chemical engineer at the University of California, Santa Barbara, pioneered "switchable surface" materials early in 2003. Such surfaces could potentially function as tiny valves in implantable devices designed as drug delivery systems or as optical waveguides that bind and release a reflective liquid coating to direct light in fiber-optic cables.

MIT assistant professor **Yoel Fink** (1999) is excited about his lab's invention of mirrored fabrics. A manufacturing process the lab developed this year combines alternating bands of polymer and glass to form a "photonic band gap" yarn that can reflect or transmit light with nanoscale precision. Fink plans to further refine his fabrics so that they might one day provide bar-code-like identifiers or transmit optical signals. In 2000 he founded OmniGuide Communications in Cambridge, MA, to develop optical-fiber technologies.

Changes of Scenery

Ethan Zuckerman (2002), cofounder of Geekcorps—a nonprofit company that sends information technology volunteers to underdeveloped countries—and TR100 Technology in the Service of Humanity award winner, has been named a fellow of the Berkman Center for Internet and Society at Harvard Law School. In July he cohosted the first Geek Activism Summit, where participants discussed ways to close the global digital divide.

Nanotechnology trailblazer **Angela Belcher** (2002) left the University of Texas at Austin last year to join MIT as an associate professor. Belcher has recently made strides in quantum dot and nanowire construction. Her process might prove the basis of self-assembling computer chips, optical devices, and biosensors.

PayPal founder and 2002 TR100 Innovator of the Year **Max Levchin** left the company in December 2002 after its sale to eBay for more than $1.5 billion. He is using his time to catch up with friends and family, and to start a new company he hopes to launch by December 2003.

Last year **Matthew Shair** (1999) became a tenured chemistry professor at Harvard University and a founding science advisor to Infinity Pharmaceuticals in Cambridge, MA. The company, with $82 million in seed funding, has made extensive use of Shair's gift for synthesizing hard-to-create compounds that can be systematically tested for their potential as pharmaceutical drugs.

Last June, Linux inventor **Linus Torvalds** (1999) went on leave from chip maker Transmeta to join Open Source Development Labs in Beaverton, OR, where he is focusing on the next version of his operating system. The organization is a nonprofit global consortium dedicated to accelerating corporate adoption of open-source software.

In March 2003 **Jackie Ying** (1999) took a leave of absence from MIT to return to her native Singapore as founding executive director of the Institute for Bioengineering and Nanotechnology. The institute is part of Biopolis, a 186,000-square-meter government center dedicated to life science research. TR

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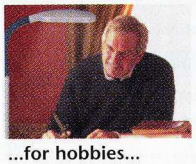

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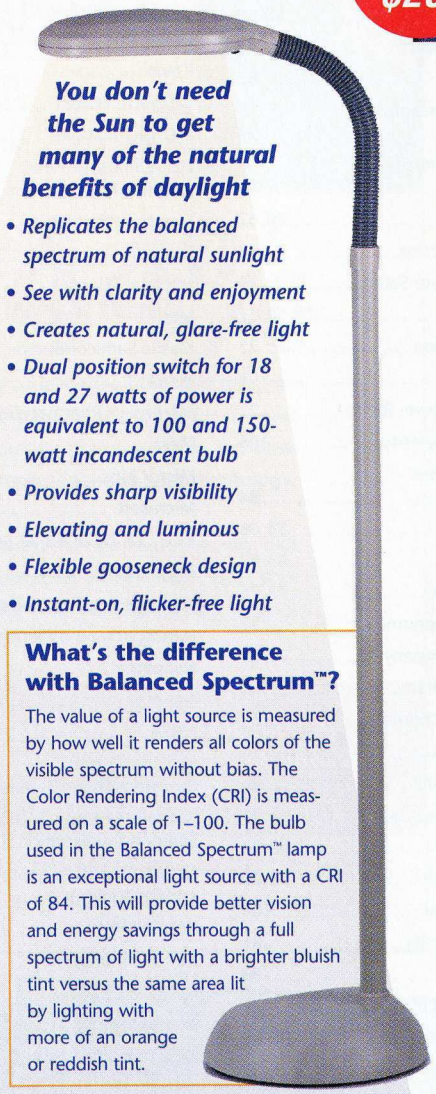

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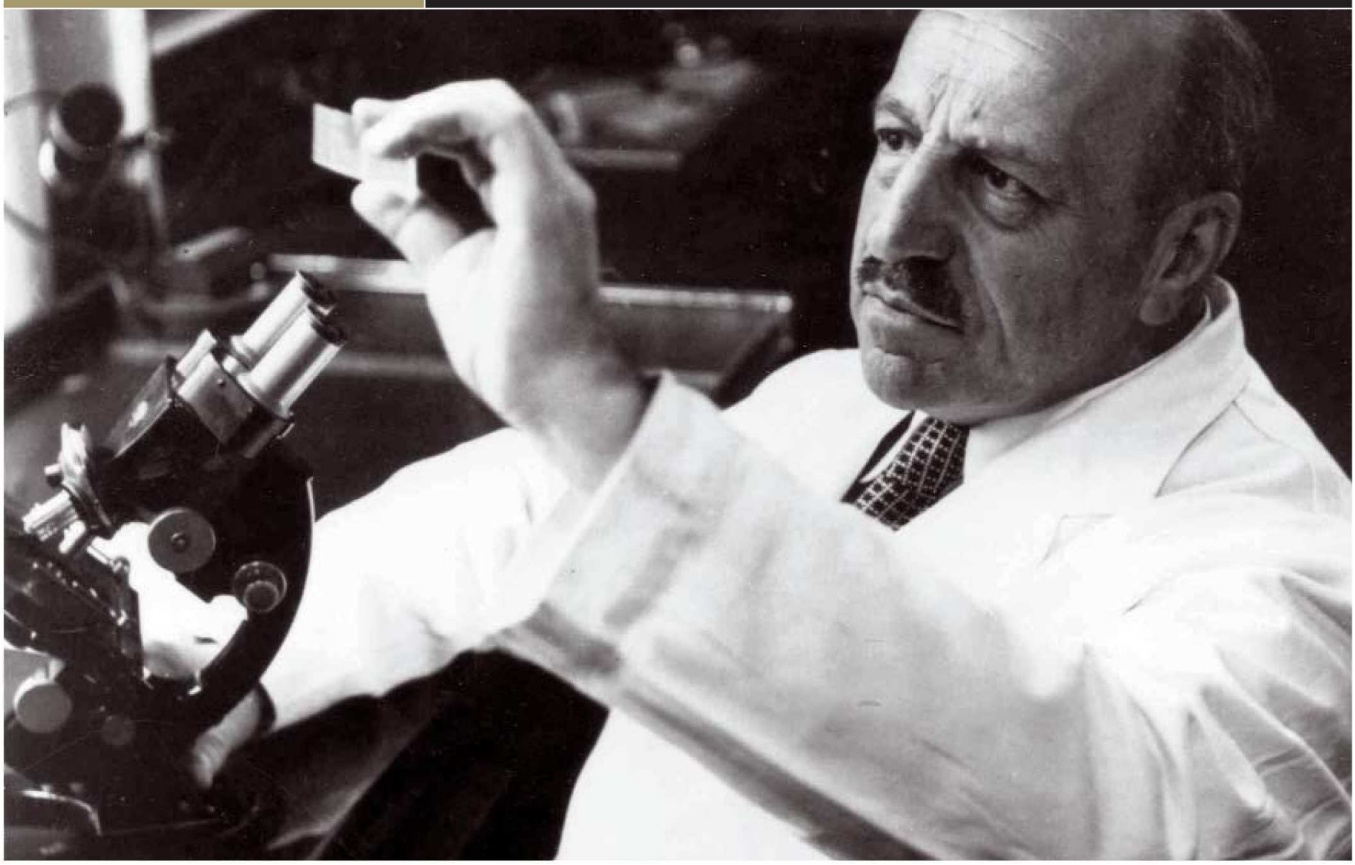

Simple Screening

Research on guinea pigs led to one of history's most effective cancer-screening tests: the Pap smear. **BY LISA SCANLON**

In 1913, George Papanicolaou arrived at Ellis Island from Greece; little did he know that within a decade he would accidentally discover one of the most effective cancer-screening tests in history. It took the medical community 20 years to adopt the simple Papanicolaou—or "Pap"—test, but once it did, the death rate associated with cervical cancer in the United States dropped more than 70 percent.

After studying medicine and zoology in Greece, Germany, and France, Papanicolaou served in the Greek Army during the Balkan War. The scientist learned about research opportunities in America from United States volunteers and decided to immigrate. During his first year in the States, he worked as a clerk for a Greek-language newspaper and played the violin at restaurants, but he was soon offered a position as a research biologist at Cornell University Medical College.

In 1916, Papanicolaou and his colleague Charles Stockard used guinea pigs' eggs to study the role of chromosomes in sex determination. In order to ascertain when the eggs were ready to be removed, Papanicolaou examined the changes in the guinea pigs' vaginal discharges by studying "smears" under a microscope. By 1923, the researcher had shifted his attention from guinea pigs to humans.

One day, while studying a sample taken from a purportedly healthy volunteer, Papanicolaou observed some abnormal cells. His interest piqued, he obtained smears from women known to have cervical cancer. The same type of cells turned up on his slides again. Papanicolaou had stumbled across a simple, relatively noninvasive way to detect cancer. Unfortunately, other doctors felt that traditional invasive biopsies were much more reliable than Papanicolaou's surface swab.

Papanicolaou persevered and found an ally in Cornell gynecologist Herbert Traut. In 1939, the pair convinced the New York Hospital to use Papanicolaou's test on all female patients. When Traut and Papanicolaou published their findings in 1943, the scientific community could no longer deny that the test was effective. The test could be easily incorporated into exams and could detect abnormal cells in their precancerous phase. In 1960, the American Cancer Society campaigned for the widespread adoption of the Pap test. Papanicolaou died two years later at age 79, after 47 years at Cornell. Today, his test is a routine part of yearly gynecological exams and has saved the lives of hundreds of thousands of women.

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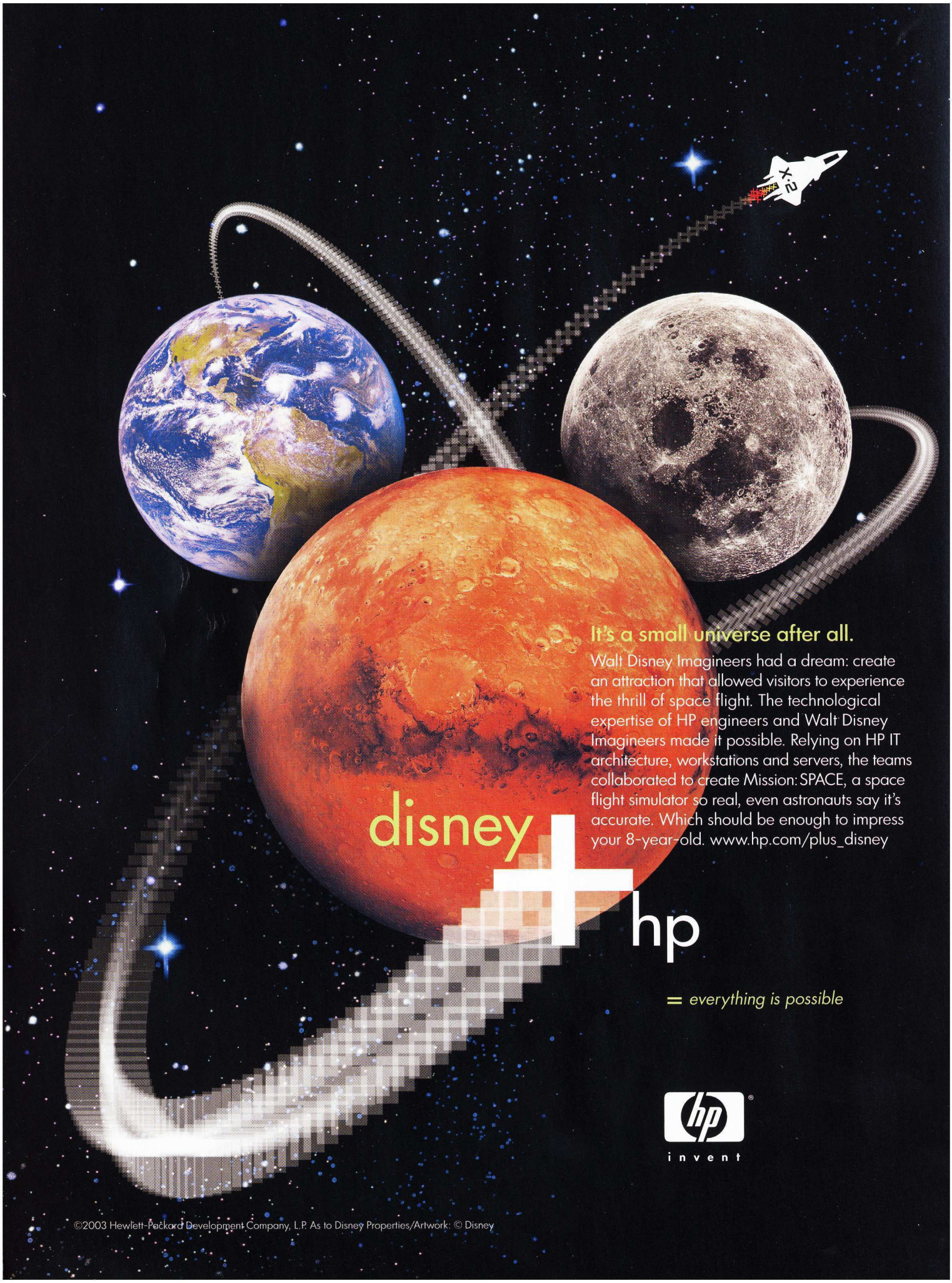
It's a small universe after all.
Walt Disney Imagineers had a dream: create an attraction that allowed visitors to experience the thrill of space flight. The technological expertise of HP engineers and Walt Disney Imagineers made it possible. Relying on HP IT architecture, workstations and servers, the teams collaborated to create Mission: SPACE, a space flight simulator so real, even astronauts say it's accurate. Which should be enough to impress your 8-year-old. www.hp.com/plus_disney
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